[1]

**TITULO / TITLE:** - A role for the Perlman syndrome exonuclease Dis3l2 in the Lin28-let-7 pathway.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Nature. 2013 May 9;497(7448):244-8. doi: 10.1038/nature12119. Epub 2013 Apr 17.

**AUTORES / AUTHORS:** - Chang HM; Triboulet R; Thornton JE; Gregory RI

**INSTITUCIÓN / INSTITUTION:** - Stem Cell Program, Boston Children's Hospital, Massachusetts 02115, USA.

**RESUMEN / SUMMARY:** - The pluripotency factor Lin28 blocks the expression of let-7 microRNAs in undifferentiated cells during development, and functions as an oncogene in a subset of cancers. Lin28 binds to let-7 precursor (pre-let-7) RNAs and recruits 3’ terminal uridylyl transferases to selectively inhibit let-7 biogenesis. Uridylated pre-let-7 is refractory to processing by Dicer, and is rapidly degraded by an unknown RNase. Here we identify Dis3l2 as the 3’-5’ exonuclease responsible for the decay of uridylated pre-let-7 in mouse embryonic stem cells. Biochemical reconstitution assays show that 3’ oligouridylation stimulates Dis3l2 activity in vitro, and knockdown of Dis3l2 in mouse embryonic stem cells leads to the stabilization of pre-let-7. Our study establishes 3’ oligouridylation as an RNA decay signal for Dis3l2, and identifies the first physiological RNA substrate of this new exonuclease, which is mutated
in the Perlman syndrome of fetal overgrowth and causes a predisposition to Wilms’ tumour development.

[2]

**TÍTULO / TITLE:** - Intermittent versus continuous androgen deprivation in prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Hussain M; Tangen CM; Berry DL; Higano CS; Crawford ED; Liu G; Wilding G; Prescott S; Kanaga Sundaram S; Small EJ; Dawson NA; Donnelly BJ; Venner PM; Vaishampayan UN; Schellhammer PF; Quinn DI; Raghavan D; Ely B; Moinpour CM; Vogelzang NJ; Thompson IM Jr

**INSTITUCIÓN / INSTITUTION:** - University of Michigan, Division of Hematology/Oncology, 1500 E Medical Center Dr., 7314 CC, Ann Arbor, MI 48109-0946, USA. mahahuss@umich.edu

**RESUMEN / SUMMARY:** - BACKGROUND: Castration resistance occurs in most patients with metastatic hormone-sensitive prostate cancer who are receiving androgen-deprivation therapy. Replacing androgens before progression of the disease is hypothesized to prolong androgen dependence. METHODS: Men with newly diagnosed, metastatic, hormone-sensitive prostate cancer, a performance status of 0 to 2, and a prostate-specific antigen (PSA) level of 5 ng per milliliter or higher received a luteinizing hormone-releasing hormone analogue and an antiandrogen agent for 7 months. We then randomly assigned patients in whom the PSA level fell to 4 ng per milliliter or lower to continuous or intermittent androgen deprivation, with patients stratified according to prior or no prior hormonal therapy, performance status, and extent of disease (minimal or extensive). The coprimary objectives were to assess whether intermittent therapy was noninferior to continuous therapy with respect to survival, with a one-sided test with an upper boundary of the hazard ratio of 1.20, and whether quality of life differed between the groups 3 months after randomization.

**RESULTADOS:** A total of 3040 patients were enrolled, of whom 1535 were included in the analysis: 765 randomly assigned to continuous androgen deprivation and 770 assigned to intermittent androgen deprivation. The median follow-up period was 9.8 years. Median survival was 5.8 years in the continuous-therapy group and 5.1 years in the intermittent-therapy group (hazard ratio for death with intermittent therapy, 1.10; 90% confidence interval, 0.99 to 1.23). Intermittent therapy was associated with better erectile function and mental health (P<0.001 and P=0.003, respectively) at month 3 but not thereafter. There were no significant differences between the groups in the number of treatment-related high-grade adverse events. CONCLUSION: Our findings were statistically
inconclusive. In patients with metastatic hormone-sensitive prostate cancer, the confidence interval for survival exceeded the upper boundary for noninferiority, suggesting that we cannot rule out a 20% greater risk of death with intermittent therapy than with continuous therapy, but too few events occurred to rule out significant inferiority of intermittent therapy. Intermittent therapy resulted in small improvements in quality of life. (Funded by the National Cancer Institute and others; ClinicalTrials.gov number, NCT00002651.).

[3]

**TÍTULO / TITLE:** - The impact of intravesical Gemcitabine and 1/3 dose Bacillus Calmette Guerin instillation therapy on the quality of life in non-muscle-invasive bladder cancer patients: results of a prospective, randomised phase II trial.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Gontero P; Oderda M; Mehnert A; Gurioli A; Marson F; Lucca I; Rink M; Schmid M; Kluth LA; Pappagallo G; Sogni F; Sanguedolce F; Schiavina R; Martorana G; Shariat SF; Chun F

**INSTITUCIÓN / INSTITUTION:** - University of Turin, Department of Urology, University of Turin, A.O.U. San Giovanni Battista, Turin, Italy. Electronic address: paolo.gontero@unito.it

**RESUMEN / SUMMARY:** - PURPOSE: BCG and intravesical chemotherapy represent viable adjuvant options in intermediate-risk non-muscle-invasive bladder cancer (NMIBC). Although BCG is perceived as less tolerable than intravesical chemotherapy, no comparative studies have addressed quality of life (QoL) issues. We compared QoL of NMIBC patients who received either adjuvant intravesical gemcitabine or 1/3 dose BCG. MATERIAL AND METHODS: our multicenter, prospective, randomised, phase II study included 120 intermediate-risk NMIBC; 88 remained assessable at 1-year follow-up. Only one patient was withdrawn because of adverse events. 61 patients received gemcitabine 2000 mg/50 cc weekly for 6 weeks (maintenance monthly for one year), while 59 BCG Connaught 1/3 dose weekly for 6 weeks (maintenance 3 weekly instillations at 3, 6 and 12 months). QoL was measured by EORTC QLQ-C30 and BLS-24 questionnaires. Group differences were calculated using analysis of variance (ANOVA/MANOVA). RESULTS: treatment was well-tolerated in both groups, although local and systemic side-effects were more frequent in the BCG-arm. Multivariable analyses showed no significant differences between the two groups in all QoL dimensions. No significant changes over time in QoL domains were detected for both BCG and gemcitabine patients, except for Physical Functioning, which significantly decreased in both groups (p 0.002). No significant differences were detected in
terms of recurrence and progression between the two groups at 1 year follow-up. CONCLUSIONS: while a higher rate of side effects, albeit mild to moderate, was detected with 1/3 dose BCG as compared to gemcitabine, our study failed to show significant differences between the two drugs in terms of QoL.

[4]

TÍTULO / TITLE: - Multi-institutional Prospective Evaluation of Bowel Quality of Life After Prostate External Beam Radiation Therapy Identifies Patient and Treatment Factors Associated With Patient-Reported Outcomes: The PROSTQA Experience.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hamstra DA; Conlon AS; Daignault S; Dunn RL; Sandler HM; Hembroff AL; Zietman AL; Kaplan I; Ciezki J; Kuban DA; Wei JT; Sanda MG; Michalski JM

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, The University of Michigan Medical Center, Ann Arbor, Michigan. Electronic address: dhamm@med.umich.edu.

RESUMEN / SUMMARY: - PURPOSE: To evaluate patients treated with external beam radiation therapy as part of the multicenter Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment (PROSTQA), to identify factors associated with posttreatment patient-reported bowel health-related quality of life (HRQOL). METHODS AND MATERIALS: Pretreatment characteristics and treatment details among 292 men were evaluated using a general linear mixed model for their association with measured HRQOL by the Expanded Prostate Cancer Index Composite instrument through 2 years after enrollment. RESULTS: Bowel HRQOL had a median score of 100 (interquartile range 91.7-100) pretreatment and 95.8 (interquartile range 83.3-100) at 2 years, representing new moderate/big problems in 11% for urgency, 7% for frequency, 4% for bloody stools, and 8% for an overall bowel problems. Baseline bowel score was the strongest predictor for all 2-year endpoints. In multivariable models, a volume of rectum >/=25% treated to 70 Gy (V70) yielded a clinically significant 9.3-point lower bowel score (95% confidence interval [CI] 16.8-1.7, P=.015) and predicted increased risks for moderate to big fecal incontinence (P=.0008). No other radiation therapy treatment-related variables influenced moderate to big changes in rectal HRQOL. However, on multivariate analyses V70 >/=25% was associated with increases in small, moderate, or big problems with the following: incontinence (3.9-fold; 95% CI 1.1-13.4, P=.03), rectal bleeding (3.6-fold; 95% CI 1.3-10.2, P=.018), and bowel urgency (2.9-fold; 95%
CI 1.1-7.6, P=.026). Aspirin use correlated with a clinically significant 4.7-point lower bowel summary score (95% CI 9.0-0.4, P=.03) and an increase in small, moderate, or big problems with bloody stools (2.8-fold; 95% CI 1.2-6.4, P=.018). Intensity modulated radiation therapy was associated with higher radiation therapy doses to the prostate and lower doses to the rectum but did not independently correlate with bowel HRQOL. CONCLUSION: After contemporary dose-escalated external beam radiation therapy up to 11% of patients have newly identified moderate/big problems with bowel HRQOL 2 years after treatment. Bowel HRQOL is related to baseline function, rectal V70, and aspirin use. Finally, our findings validate the commonly utilized cut-point of rectal V70 >/=25% as having significant impact on patient-reported outcomes.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.eururo.2013.03.021
AUTORES / AUTHORS: - Duthie JB; Murphy DG
INSTITUCIÓN / INSTITUTION: - Division of Cancer Surgery, Peter MacCallum Cancer Centre, Melbourne, Australia.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.145
AUTORES / AUTHORS: - Cella D; Escudier B; Rini B; Chen C; Bhattacharyya H; Tarazi J; Rosbrook B; Kim S; Motzer R
INSTITUCIÓN / INSTITUTION: - Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, 633 N. St, Clair - 19th Floor Chicago, IL 60611, USA.
RESUMEN / SUMMARY: - Background:Axitinib demonstrated greater progression-free survival vs sorafenib in a phase III study of previously treated patients with metastatic renal cell carcinoma. Here, we report patient-reported kidney-specific symptoms and health status, measured by the Functional Assessment of
Cancer Therapy (FACT) Kidney Cancer Symptom Index (FKSI) and the European Quality of Life self-report questionnaire (EQ-5D). Methods: In all, 723 patients received axitinib (starting dose 5 mg twice daily (b.i.d.)) or sorafenib (400 mg b.i.d.). The FKSI-15, including the disease-related symptoms (FKSI-DRS) subscale, was administered on day 1 before dosing, every 4 weeks and at end of treatment (EOT)/withdrawal. Statistical methods included a mixed-effects repeated-measures model. Results: At baseline, patients in both arms had relatively high mean FKSI-15 and FKSI-DRS scores, comparable to the general US population. Subsequent on-treatment overall mean scores were similar between axitinib and sorafenib, and there was no substantial decline during treatment. Scores substantially worsened at EOT, mainly due to disease progression. Conclusion: Patient-reported outcomes were comparable for second-line axitinib and sorafenib and were maintained at relatively high levels while on treatment, but worsened at EOT. As duration of treatment was longer with axitinib than sorafenib, time to worsening of symptoms can be delayed longer with axitinib.

[7]
TÍTULO / TITLE: Identification of nine new susceptibility loci for testicular cancer, including variants near DAZL and PRDM14.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Ruark E; Seal S; McDonald H; Zhang F; Elliot A; Lau K; Perdeaux E; Rapley E; Eeles R; Peto J; Kote-Jarai Z; Muir K; Nsengimana J; Shipley J; Bishop DT; Stratton MR; Easton DF; Huddart RA; Rahman N; Turnbull C
INSTITUCIÓN / INSTITUTION: Division of Genetics and Epidemiology, Institute of Cancer Research, Sutton, UK.
RESUMEN / SUMMARY: Testicular germ cell tumor (TGCT) is the most common cancer in young men and is notable for its high familial risks. So far, six loci associated with TGCT have been reported. From genome-wide association study (GWAS) analysis of 307,291 SNPs in 986 TGCT cases and 4,946 controls, we selected for follow-up 694 SNPs, which we genotyped in a further 1,064 TGCT cases and 10,082 controls from the UK. We identified SNPs at nine new loci (1q22, 1q24.1, 3p24.3, 4q24, 5q31.1, 8q13.3, 16q12.1, 17q22 and 21q22.3) showing association with TGCT (P < 5 x 10⁻⁸), which together account for an additional 4-6% of the familial risk of TGCT. The loci include genes plausibly related to TGCT development. PRDM14, at 8q13.3, is essential for early germ cell specification, and DAZL, at 3p24.3, is required for the regulation of germ cell development. Furthermore, PITX1, at 5q31.1, regulates
TERT expression and is the third TGCT-associated locus implicated in telomerase regulation.

[8]

**Título / Title:** - A phase II trial of dasatinib in patients with metastatic castration-resistant prostate cancer treated previously with chemotherapy.

**Resumen / Summary:** - Enlace al Resumen / Link to its Summary


**Autores / Authors:** - Twardowski PW; Beumer JH; Chen CS; Kraft AS; Chatta GS; Mitsuhashi M; Ye W; Christner SM; Lilly MB

**Institución / Institution:** - aDepartment of Medical Oncology and Therapeutics Research, City of Hope National Medical Center, Duarte bLoma Linda University Cancer Center, Division of Hematology/Oncology, Loma Linda cHitachi Chemical Research Center dChao Family Comprehensive Cancer Center, Division of Hematology/Oncology, University of California, Irvine, California eDepartment of Pharmaceutical Sciences, University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania fMedical University of South Carolina Hollings Cancer Center, Division of Hematology/Oncology, Charleston, South Carolina, USA.

**Resumen / Summary:** - There is a need for efficacious therapies for metastatic castration-resistant prostate cancer (mCRPC) after disease progression on docetaxel. The SRC tyrosine kinase and its related family members may be important drivers of prostate cancer and can be inhibited by dasatinib. mCRPC patients, after one previous chemotherapy, started dasatinib at 70 mg twice daily, amended to 100 mg daily. The primary endpoint was the disease control (DC) rate, defined as complete response (CR), partial response (PR), or stable disease (SD) in prostate specific antigen (PSA), RECIST, bone scan, and FACT-P score. Up to 41 patients were to be accrued (two-stage design, 21+20) to rule out a null-hypothesized effect of 5 versus 20% (alpha=0.05, beta=0.1). Secondary endpoints included progression-free survival, toxicity, and pharmacokinetic and pharmacodynamic correlatives. Of 38 patients, 27 were evaluable for response or toxicity. The median duration of therapy was 55 days (6-284). Five patients showed DC after 8 weeks of therapy (18.5% DC, 95% CI: 6.3-38.1%). One PR (3.7% response rate, 95% CI: 0.1-19.0%) was observed in a patient treated for 284 days. Twelve patients (43%) discontinued treatment for toxicity. Dasatinib induced a decrease in phytohemagglutinin-stimulated CSF2, CD40L, GZMB, and IL-2 mRNAs in blood cells, indicating target engagement. Decreases in plasma IL-6 and bone alkaline phosphatase, and in urinary N-telopeptide, were associated with DC. Dasatinib has definite but limited activity in advanced mCRPC, and was poorly tolerated. The observation of a patient
with prolonged, objective, clinically significant benefit warrants molecular profiling to select the appropriate patient population.

[9]
**TÍTULO / TITLE:** Re: effect of abiraterone acetate and prednisone compared with placebo and prednisone on pain control and skeletal-related events in patients with metastatic castration-resistant prostate cancer: exploratory analysis of data from the COU-AA-301 randomised trial.

**RESUMEN / SUMMARY:** [Enlace al Resumen / Link to its Summary]


**AUTORES / AUTHORS:** Taneja SS

[10]
**TÍTULO / TITLE:** Phase III Trials With Docetaxel-Based Combinations for Metastatic Castration-Resistant Prostate Cancer: Time to Learn From Past Experiences.

**RESUMEN / SUMMARY:** [Enlace al Resumen / Link to its Summary]


**AUTORES / AUTHORS:** Antonarakis ES; Eisenberger MA

**INSTITUCIÓN / INSTITUTION:** Bunting-Blaustein Cancer Research Building 1, 1650 Orleans St, Room 1M51, Baltimore, MD 21287; eisenma@jhmi.edu

[11]
**TÍTULO / TITLE:** Re: dutasteride treatment over 2 years delays prostate-specific antigen progression in patients with biochemical failure after radical therapy for prostate cancer: results from the randomised, placebo-controlled avodart after radical therapy for prostate cancer study (ARTS).

**RESUMEN / SUMMARY:** [Enlace al Resumen / Link to its Summary]


**AUTORES / AUTHORS:** Taneja SS

[12]
TÍTULO / TITLE: Improved patient survival with simultaneous pancreas and kidney transplantation in recipients with diabetic end-stage renal disease.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Lindahl JP; Hartmann A; Horneland R; Holdaas H; Reisaeter AV; Midtvedt K; Leivestad T; Oyen O; Jenssen T

INSTITUCIÓN / INSTITUTION: Department of Transplant Medicine, Section of Nephrology, Oslo University Hospital, Rikshospitalet, Sognsvannsveien 20, 0372, Oslo, Norway, j.p.h.lindahl@medisin.uio.no.

RESUMEN / SUMMARY: AIMS/HYPOTHESIS: We aimed to determine whether simultaneous pancreas and kidney (SPK) transplantation would improve patient and kidney graft survival in diabetic end-stage renal disease (ESRD) compared with kidney transplantation alone (KTA). METHODS: Follow-up data were retrieved for all 630 patients with diabetic ESRD who had received SPK or KTA at our centre from 1983 to the end of 2010. Recipients younger than 55 years of age received either an SPK (n = 222) or, if available, a single live donor kidney (LDK; n = 171). Older recipients and recipients with greater comorbidity received a single deceased donor kidney (DDK; n = 237). Survival was analysed by the Kaplan-Meier method and in multivariate Cox regression analysis adjusting for recipient and donor characteristics. RESULTS: Patient survival was superior in SPK compared with both LDK and DDK recipients in univariate analysis. Follow-up time (mean +/- SD) after transplantation was 7.1 +/- 5.7 years. Median actuarial patient survival was 14.0 years for SPK, 11.5 years for LDK and 6.7 years for DDK recipients. In multivariate analyses including recipient age, sex, treatment modality, time on dialysis and era, SPK transplantation was protective for all-cause mortality compared with both LDK (p = 0.02) and DDK (p = 0.029) transplantation. After the year 2000, overall patient survival improved compared with previous years (HR 0.40, 95% CI 0.30, 0.55; p < 0.001). Pancreas graft survival also improved after 2000, with a 5 year graft survival rate of 78% vs 61% in previous years (1988-1999). CONCLUSIONS/INTERPRETATION: Recipients of SPK transplants have superior patient survival compared with both LDK and DDK recipients, with improved results seen over the last decade.

[13]

TÍTULO / TITLE: Re: early salvage radiation therapy combined with short-term hormonal therapy in recurrent prostate cancer after radical prostatectomy: single-institution 4-year data on outcome, toxicity, health-related quality of life and co-morbidities from 184 consecutive patients treated with 70 gy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.02.3218

AUTORES / AUTHORS: - Taneja SS


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.04.031

AUTORES / AUTHORS: - Skinner EC; Goldman B; Sakr WA; Petrylak DP; Lenz HJ; Lee CT; Wilson SS; Benson M; Lerner SP; Tangen CM; Thompson IM
INSTITUCIÓN / INSTITUTION: - Stanford University, Stanford, CA. Electronic address: skinnere@stanford.edu.

RESUMEN / SUMMARY: - PURPOSE: Prior phase II studies of intravesical gemcitabine have shown it to be active and well tolerated, but durable responses in patients with NMIBC who have recurred following BCG are uncommon. We performed a multi-institutional phase II study within the SWOG cooperative group to evaluate the potential role of gemcitabine induction plus maintenance therapy in this setting. MATERIALS AND METHODS: Eligible patients had recurrent NMIBC, stage Tis (CIS), T1, Ta high-grade (HG), or multifocal Ta low-grade, following at least 2 prior courses of BCG. Patients were treated with 2gm gemcitabine in 100cc NS intravesically weekly x6 and then
monthly to 12 months. Cystoscopy and cytology were performed every 3 months, with biopsy at 3 months and then as clinically indicated. Initial complete response was defined as negative cystoscopy, cytology and biopsy at 3 months. RESULT5: 558 patients were enrolled; and 47 were evaluable for response. 42 (89%) of the evaluable patients had high-risk disease, HGTa in 12 (26%), HGT1 in 2 (4%), and CIS in 28 (60%) +/- papillary lesions. At the initial 3-month evaluation, 47% of patients were free of disease. At one year 28% of the 47 patients had not recurred, all except 2 from the high-risk group, and 21% at 2 years. CONCLUSION: Intravesical gemcitabine has activity in high risk NMIBC, and offers an option for patients who have recurred after BCG and are not suitable for cystectomy. However, less than 30% of patients had durable response at 12 months, even with maintenance therapy.

[16] TÍTULO / TITLE: - Interval to Biochemical Failure Predicts Clinical Outcomes in Patients With High-Risk Prostate Cancer Treated by Combined-Modality Radiation Therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Shilkrut M; McLaughlin PW; Merrick GS; Vainshtein JM; Feng FY; Hamstra DA
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Michigan Health System, Ann Arbor, Michigan.
RESUMEN / SUMMARY: - PURPOSE: To validate the prognostic value of interval to biochemical failure (IBF) in patients with high-risk prostate cancer (HiRPCa) treated with combined-modality radiation therapy (CMRT) with or without androgen deprivation therapy (ADT). METHODS AND MATERIALS: We conducted a retrospective review of HiRPCa (prostate-specific antigen >20 ng/mL, Gleason score [GS] 8-10, or clinical T stage T3-T4) treated with either dose-escalated external beam radiation therapy (EBRT) or CMRT. Interval to biochemical failure was classified as </=18 or >18 months from the end of all therapy to the date of biochemical failure (BF). Kaplan-Meier methods and Cox proportional hazards regression were used to evaluate the prognostic value of IBF </=18 months for distant metastasis (DM) and prostate cancer-specific mortality (PCSM). RESULTS: Of 958 patients with a median follow-up of 63.2 months, 175 patients experienced BF. In those with BF, there were no differences in pretreatment clinical characteristics between the EBRT and CMRT groups, except for a higher proportion of patients with GS 8-10 in the CMRT group (70% vs 52%, P=.02). Median IBF after all therapy was 24.0
months (interquartile range 9.6-46.0) in the EBRT group and 18.9 months (interquartile range 9.2-34.5) in the CMRT group (P=.055). On univariate analysis, IBF $\leq$18 months was associated with increased risk of DM and PCSM in the entire cohort and the individual EBRT and CMRT groups. On multivariate analysis, only GS 9-10 and IBF $\leq$18 months, but not the radiation therapy regimen or ADT use, predicted DM (hazard ratio [HR] 3.7, P<.01, 95% confidence interval [CI] 1.4-10.3 for GS 9-10; HR 3.9, P<.001, 95% CI 2.4-6.5 for IBF $\leq$18 months) and PCSM (HR 14.8, P<.009, 95% CI 2.0-110 for GS 9-10; HR 4.4, P<.0001, 95% CI 2.4-8.1 for IBF $\leq$18 months). CONCLUSIONS: Short IBF was highly prognostic for higher DM and PCSM in patients with HiRPCa. The prognostic value of IBF for DM and PCSM was not affected by the radiation therapy regimen or ADT use.

[17]
TÍTULO / TITLE: - Patient-reported genitourinary toxicity for long-term prostate cancer survivors treated with radiation therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Olsson CE; Pettersson N; Alsadius D; Wilderang U; Tucker SL; Johansson KA; Steineck G
INSTITUCIÓN / INSTITUTION: - Division of Clinical Cancer Epidemiology, Department of Oncology, Institute of Clinical Sciences, Sahlgrenska Academy at University of Gothenburg, Goteborg, Sweden.
RESUMEN / SUMMARY: - Background:The objective of this study is to provide comprehensive overviews of patient-reported urinary symptoms for long-term prostate cancer survivors treated with radiation therapy and for untreated, healthy men.Methods:We performed a population-based cross-sectional study using a study-specific postal questionnaire assessing symptoms among 1007 men consecutively treated at the Sahlgrenska University Hospital, Goteborg, Sweden from 1993-2006 (primary or salvage external beam radiation therapy (EBRT) or EBRT and high-dose rate brachytherapy). We also randomly recruited 350 non-pelvic-irradiated matched control men from the Swedish Total Population Register. Symptom prevalence and prevalence ratios were computed.Results:Survey participation rate was 89% (874/985) for eligible survivors and 73% (243/332) for eligible controls. Median time from treatment to follow-up was 5 years (range, 1-14 years). Among the 21 investigated symptoms reflecting obstruction, frequency, urgency, pain and incontinence, we found significantly higher prevalence compared with controls for 9 symptoms in the EBRT group, 10 in the EBRT+brachytherapy group and 5 in the salvage EBRT group. The prevalence for a majority of the symptoms was stable over
Conclusion: The presented toxicity profiles provide a thorough understanding of patient-reported urinary symptoms that can assist in developing personalised therapy for prostate cancer.

[18]
**TÍTULO / TITLE:** A heart of stone: rapid metastatic cardiac calcification in an end-stage renal disease patient.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** Salamon JN; Garcia MJ; Guelfguat M; Meisner JS
**INSTITUCIÓN / INSTITUTION:** Department of Medicine, Albert Einstein College of Medicine/Jacobi Medical Center, Bronx, New York.

[19]
**TÍTULO / TITLE:** A Phase II Trial of Neoadjuvant nab-paclitaxel, Carboplatin, and Gemcitabine (ACaG) in Patients With Locally Advanced Carcinoma of the Bladder.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** Grivas PD; Hussain M; Hafez K; Daignault-Newton S; Wood D; Lee CT; Weizer A; Montie JE; Hollenbeck B; Montgomery JS; Alva A; Smith DC
**INSTITUCIÓN / INSTITUTION:** Department of Internal Medicine, Division of Hematology/Oncology, Ann Arbor, MI.
**RESUMEN / SUMMARY:** OBJECTIVE: To assess the activity of neoadjuvant nab-paclitaxel, carboplatin, gemcitabine (ACaG) followed by cystectomy in patients with muscle-invasive urothelial carcinoma of the bladder. METHODS: Patients who were candidates for cystectomy received nab-paclitaxel 260 mg/m² on day 1, carboplatin area under the curve 5 on day 1, and gemcitabine 800 mg/m² on days 1 and 8, every 21 days for 3 cycles. The first 3 patients received nab-paclitaxel 100 mg/m² weekly and were not included in the efficacy analysis of evaluable patients. Efficacy was assessed by the percentage of patients with pathologic complete response (pT0) at cystectomy. Progression-free and overall survival was estimated using the Kaplan-Meier methods. RESULTS: Of 29 patients enrolled, 26 received the planned 3 cycles with 82 cycles overall; doses were reduced in 16 patients. Of 29 patients, nearly all patients
experienced grade 3-4 neutropenia; 17 patients (58.6%) required growth factor, and 16 patients (55.2%) experienced grade 3-4 thrombocytopenia; there was 1 toxicity-related death. Nonhematological toxicity was generally tolerable. Twenty-two of 26 patients were evaluable for the primary endpoint: 6 patients (27.3%, 95% confidence interval [CI] 10.7-50.2) had pT0, 6 pTis, 1 pT1, 54.5% of patients had no residual muscle-invasive disease (<pT2N0), and 81.8% had pN0 at cystectomy. By intent-to-treat (ITT) analysis, the pT0 rate was 27.6% (95% CI 12.7-47.2). CONCLUSION: Neoadjuvant nab-paclitaxel, carboplatin, gemcitabine is feasible but grade 3-4 myelotoxicity is common. Although the regimen has activity, the pT0 rate is lower than those reported with cisplatin-based regimens and did not meet the predefined threshold to support further investigation. Taxane-based regimens remain investigational for neoadjuvant therapy of bladder cancer.

[20]

**TITULO / TITLE:** - A phase II trial of androgen deprivation therapy (ADT) plus chemotherapy as initial treatment for local failures or advanced prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2163-4

**AUTORES / AUTHORS:** - Amato R; Stepankiw M; Gonzales P

**INSTITUCIÓN / INSTITUTION:** - Division of Oncology, Department of Internal Medicine, University of Texas Health Science Center at Houston (Medical School)/Memorial Hermann Cancer Center, 6410 Fannin St., Suite 830, Houston, TX, 77030, USA, robert.amato@uth.tmc.edu.

**RESUMEN / SUMMARY:** - PURPOSE: Long-term hormonal ablation in prostate cancer is associated with decreased overall health and quality of life. Few reports emphasized the role of chemotherapy in the management of early stage prostate cancer. This study analyzed the safety and efficacy of androgen deprivation therapy (ADT) plus chemotherapy as initial treatment for patients identified as local failures or not eligible for prostatectomy or radiation therapy due to advanced disease presentation. METHODS: Enrolled patients received ADT in the form of leuprolide every 12 weeks for 24 months with bicalutamide initiating after the completion of chemotherapy. Chemotherapy consisted of ketoconazole and doxorubicin for weeks 1, 3, and 5 and estramustine and docetaxel and for weeks 2, 4 and 6. During weeks 7 and 8, no treatment was received. RESULTS: Forty-six patients were enrolled, and forty-five patients were evaluable. Median progression-free survival (PFS) was 23.4 months. Median overall survival (OS) was 53.7 months. Out of 45 patients with measurable disease, 22 patients had an objective response: 9 patients
achieved a complete response; 2 patients achieved a partial response; 10 patients achieved stable disease. Frequent grade 3 adverse events included elevated ALT (17 %), hypokalemia (13 %), and hypophosphatemia (13 %). Grade 4 adverse events were rare and included low bicarbonate (2 %), hypokalemia (2 %), leukocytopenia (2 %), and neutropenia (2 %).

CONCLUSIONS: The treatment demonstrated clinical benefit in all patient subsets with minimal reversible treatment-related adverse events. Subgroup analysis suggests that having prior local therapy resulted in greater PFS and OS.

[21]

[21]

TÍTULO / TITLE: - Stable renal engraftment in a patient following successful tandem autologous/reduced-intensity conditioning allogeneic transplantation for treatment of multiple myeloma with del(17p) that developed as a post-transplantation lymphoproliferative disease following renal transplantation.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Aoki T; Kasai M; Harada Y; Matsubara E; Morishita T; Suzuki T; Tsujita M; Goto N; Katayama A; Watarai Y; Uchida K; Ito M; Saji H; Tsuzuki T; Uchida T; Ogura M

INSTITUCIÓN / INSTITUTION: - Department of Hematology and Oncology, Nagoya Daini Red Cross Hospital, 2-9 Myoken-cho, Showa-ku, Nagoya, 466-8650, Japan.

RESUMEN / SUMMARY: - Multiple myeloma (MM) developing after renal transplantation is rare. From January 1972 to December 2011, a total of 1,485 patients underwent renal transplantation in Nagoya Daini Red Cross Hospital; 14 (0.9 %) of these recipients developed post-transplantation lymphoproliferative disorders (PTLDs) including two plasma cell neoplasms. Here, we report the clinical course of a 35-year-old male with immunoglobulin G k-type MM of recipient origin that developed 5 years after renal transplantation from a human leukocyte antigen (HLA)-haploidentical female sibling donor, which was performed to address dialysis-dependent chronic glomerulonephritis. Cytogenetic analysis revealed significant del(17p) abnormalities in myeloma cells. After non-response to bortezomib treatment, the patient achieved partial response with a thalidomide-containing salvage regimen and underwent successful tandem autologous/reduced-intensity conditioning allogeneic hematopoietic stem cell transplantation (HSCT) from an unrelated male donor matched for seven of eight HLAs. At the 8-month follow-up time point, the patient’s performance status remained good, and the transplanted kidney remains functional without rejection. To the best of our knowledge, this is the
first report of a successful use of allogeneic HSCT for a patient who developed MM as a PTLD after renal transplantation. This patient has a transplanted kidney and transplanted hematopoietic cells that currently coexist without rejection.

[22]

**TÍTULO / TITLE:** - The Prostate Cancer Prevention Trial risk calculator and the relationship between prostate-specific antigen and biopsy outcome.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Vickers AJ; Sjoberg DD; Ankerst DP; Tangen CM; Goodman PJ; Thompson Jr IM

**INSTITUCIÓN / INSTITUTION:** - Memorial Sloan-Kettering Cancer Center, New York, New York.

**RESUMEN / SUMMARY:** - BACKGROUND: The Prostate Cancer Prevention Trial (PCPT) Risk Calculator is a widely used prediction tool for aiding decisions about biopsy for prostate cancer. This study hypothesized that recently reported differences between predictions from the model and findings from other cohorts were due to how prostate-specific antigen (PSA) was entered into the statistical model, and to the inclusion of protocol end-of-study biopsies for which there was no clinical indication. METHODS: Data was obtained from the 5088 PCPT participants and was used to construct the PCPT Risk Calculator. The relationship between PSA and the risk of a positive biopsy was modeled by using locally-weighted regression (loess), an empirical estimate of actual risks observed which does not depend on a statistical model. Risks were estimated with and without the 3514 end-of-study biopsies. RESULTS: For PSA levels above biopsy thresholds (approximately 4 ng/mL), the PCPT Risk Calculator greatly overestimated actual empirical risks (eg, 44% versus 26% at 5 ng/mL). The change in risk with increasing PSA was less among for-cause biopsies compared with the end-of-study biopsies (P = .001). Risk of high-grade disease was overestimated at PSA level of >/= 6 ng/mL. CONCLUSIONS: The PCPT Risk Calculator overestimates risks for PSAs close to and above typical biopsy thresholds. Separating for-cause biopsies from end-of-study biopsies and using empirical rather than model-based risks reduces overall risk estimates and replicates prior findings that, in men who have been screened with PSA, there is no rapid increase in prostate cancer risk with higher PSA. Revision of the PCPT Risk Calculator should be considered. Cancer 2013. © 2013 American Cancer Society.

[23]
Polymorphisms in the XRCC1 gene modify survival of bladder cancer patients treated with chemotherapy.

Survival of bladder cancer patients depends on several factors including disease stage and grade at diagnosis, age, health status of the patient and the applied treatment. Several studies investigated the role of DNA repair genetic variants in cancer susceptibility, but only few studies investigated their role in survival and response to chemotherapy for bladder cancer. We genotyped 28 single nucleotide polymorphisms (SNP) in DNA repair genes in 456 bladder cancer patients, reconstructed haplotypes and calculated a score for combinations of the SNPs. We estimated Hazard Ratios (adjHR) for time to death. Among patients treated with chemotherapy, variant alleles of five SNPs in the XRCC1 gene conferred better survival (rs915927 adjHR 0.55 (95%CI 0.32-0.94); rs76507 adjHR 0.48 (95%CI 0.27-0.84); rs2854501 adjHR 0.25 (95%CI 0.12-0.52); rs2854509 adjHR 0.21 (95%CI 0.09-0.46); rs3213255 adjHR 0.46 (95%CI 0.26-0.80). In this group of patients, an increasing number of variant alleles in a XRCC1 gene score were associated with a better survival (26% decrease of risk of death for each additional variant allele in XRCC1). By functional analyses we demonstrated that the previous XRCC1 SNPs confer lower DNA repair capacity. This may support the hypothesis that survival in these patients may be modulated by the different DNA repair capacity determined by genetic variants. Chemotherapy treated cancer patients bearing an increasing number of “risky” alleles in XRCC1 gene had a better survival, suggesting that a proficient DNA repair may result in resistance to therapy and shorter survival. This finding may have clinical implications for the choice of therapy.
PURPOSE
Obesity has consistently been linked to an increased risk of colorectal cancer, particularly among men. Whether body mass index (BMI) differentially influences the risk across the stages of colorectal cancer development remains unclear. We evaluated the associations of BMI with colorectal adenoma incidence, adenoma recurrence, and cancer in the context of a large screening trial, in which cases and controls had an equal chance for disease detection.

METHODS
We prospectively evaluated the association between baseline BMI and the risk of incident distal adenoma (1,213 cases), recurrent adenoma (752 cases), and incident colorectal cancer (966 cases) among men and women, ages 55 to 74 years, randomly assigned to receive flexible sigmoidoscopy screening as part of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. We calculated odds ratios (ORs) and 95% CIs for adenoma incidence and recurrence, and hazard ratios (HRs) and 95% CIs for colorectal cancer incidence, using multivariable-adjusted models.

RESULTS
Compared with normal-weight men (18.5 to 24.9 kg/m²), obese men (≥ 30 kg/m²) had significantly higher risk of incident adenoma (OR, 1.32; 95% CI, 1.06 to 1.65) and colorectal cancer (HR, 1.48; 95% CI, 1.16 to 1.89) and a borderline increased risk of recurrent adenoma (OR, 1.50; 95% CI, 0.98 to 2.30). No associations were observed for either adenoma or cancer in women.

CONCLUSION
Data from this large prospective study suggest that obesity is important throughout the natural history of colorectal cancer, at least in men, and colorectal cancer prevention efforts should encourage the achievement and maintenance of a healthy body weight in addition to regular screenings.
**TÍTULO / TITLE:** - Phase 2 Trial of Single-agent Everolimus in Chemotherapy-naive Patients with Castration-resistant Prostate Cancer (SAKK 08/08).

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Templeton AJ; Dutoit V; Cathomas R; Rothermundt C; Bartschi D; Droge C; Gautschi O; Borner M; Fechter E; Stenner F; Winterhalder R; Muller B; Schiess R; Wild PJ; Ruschoff JH; Thalmann G; Dietrich PY; Aebersold R; Klingbiel D; Gillessen S

**INSTITUCIÓN / INSTITUTION:** - Department of Medical Oncology, Kantonsspital St. Gallen, St. Gallen, Switzerland. Electronic address: arnoud.templeton@kssg.ch.

**RESUMEN / SUMMARY:** - BACKGROUND: The phosphatase and tensin homolog (PTEN) tumor suppressor gene is deregulated in many advanced prostate cancers, leading to activation of the phosphatidylinositol 3-kinase (PI3K)-Akt-mammalian target of rapamycin (mTOR) pathway and thus increased cell survival. OBJECTIVE: To evaluate everolimus, an inhibitor of mTOR, in patients with metastatic castration-resistant prostate cancer (mCRPC), and to explore potentially predictive serum biomarkers by proteomics, the significance of PTEN status in tumor tissue, and the impact of everolimus on immune cell subpopulations and function. DESIGN, SETTING, AND PARTICIPANTS: A total of 37 chemotherapy-naive patients with mCRPC and progressive disease were recruited to this single-arm phase 2 trial (ClinicalTrials.gov identifier NCT00976755). INTERVENTION: Everolimus was administered continuously at a dose of 10mg daily. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: The primary end point was progression-free survival (PFS) at 12 wk defined as the absence of prostate-specific antigen (PSA), radiographic progression, or clinical progression. Groups were compared using Wilcoxon rank-sum tests or Fisher exact tests for continuous and discrete variables, respectively. Time-to-event end points were analyzed using the Kaplan-Meier method and univariate Cox regression. RESULTS AND LIMITATIONS: A total of 13 patients (35%; 95% confidence interval, 20-53) met the primary end point. Confirmed PSA response >/=50% was seen in two (5%), and four further patients (11%) had a PSA decline >/=30%. Higher serum levels of carboxypeptidase M and apolipoprotein B were predictive for reaching the primary end point. Deletion of PTEN was associated with longer PFS and response. Treatment was associated with a dose-dependent decrease of CD3, CD4, and CD8 T lymphocytes and CD8 proliferation and an increase in regulatory T cells. Small sample size was the major limitation of the study.
CONCLUSIONS: Everolimus activity in unselected patients with mCRPC is moderate, but PTEN deletion could be predictive for response. Several serum glycoproteins were able to predict PFS at 12 wk. Prospective validation of these potential biomarkers is warranted. TRIAL REGISTRATION: This study is registered with ClinicalTrials.gov with the identifier NCT00976755. Results of this study were presented in part at the 47th Annual Meeting of the American Society of Clinical Oncology (June 3-7, 2011; Chicago, IL, USA) and the annual meeting of the German, Austrian, and Swiss Societies for Oncology and Hematology (September 30-October 4, 2011; Basel, Switzerland).

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: May M; Aziz A; Zigeuner R; Chromecki T; Cindolo L; Schips L; De Cobelli O; Rocco B; De Nunzio C; Tubaro A; Coman I; Truss M; Dalpiaz O; Hoschke B; Gilfrich C; Feciche B; Stoltze A; Fenske F; Fritsche HM; Figenschau RS; Madison K; Sanchez-Chapado M; Martin MD; Salzano L; Lotrecchiano G; Joniau S; Waidelich R; Stief C; Brookman-May S
INSTITUCIÓN / INSTITUTION: Department of Urology, St. Elisabeth Hospital Straubing, Straubing, Germany.
RESUMEN / SUMMARY: PURPOSE: To investigate gender differences in clinicopathological features and to analyze the prognostic impact of gender in renal cell carcinoma (RCC) patients undergoing surgery. METHODS: A total of 6,234 patients (eleven centers; Europe and USA) treated by radical or partial nephrectomy were included in this retrospective study (median follow-up 59 months; IQR 30-106). Gender differences in clinicopathological parameters were assessed. Multivariable Cox regression models were applied to determine the influence of parameters on disease-specific survival (DSS) and overall survival (OS). RESULTS: A total of 3,751 patients of the study group were male patients (60.2 %), who were significantly younger at diagnosis and received more frequently NSS than women. Significantly, more often high-grade tumors and simultaneous metastasis were present in men. Whereas tumor size and pTN stages did not differ between genders, clear-cell and chromophobe RCC was diagnosed less frequently, but papillary RCC more often in men. Gender also independently influenced DSS (HR 0.75, p < 0.001) and OS (HR 0.80, p < 0.001) with a benefit for women. However, inclusion of gender in multivariable models did not significantly gain predictive accuracies (PA) for DSS (0.868-
Furthermore, no significantly different DSS and OS rates were found in patients undergoing NSS. CONCLUSIONS: This study demonstrates important gender differences in clinicopathological features and outcome of RCC patients with improved DSS and OS for women compared to men, even if solely patients with clear-cell RCC or M0-stage are taken into evaluation. However, inclusion of gender in multivariable models does not significantly gain PA of multivariable models.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.eururo.2013.03.033
AUTORES / AUTHORS: - Zumsteg ZS; Spratt DE; Pei I; Zhang Z; Yamada Y; Kollmeier M; Zelefsky MJ
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.
RESUMEN / SUMMARY: - BACKGROUND: The management of intermediate-risk prostate cancer (PCa) is controversial, in part due to the heterogeneous nature of patients falling within this classification. OBJECTIVE: We propose a new risk stratification system for intermediate-risk PCa to aid in prognosis and therapeutic decision making. DESIGN, SETTING, AND PARTICIPANTS: Between 1992 and 2007, 1024 patients with National Comprehensive Cancer Network intermediate-risk PCa and complete biopsy information were treated with definitive external-beam radiation therapy (EBRT) utilizing doses >/=81Gy. Unfavorable intermediate-risk (UIR) PCa was defined as any intermediate-risk patient with a primary Gleason pattern of 4, percentage of positive biopsy cores (PPBC) >/=50%, or multiple intermediate-risk factors (IRFs; cT2b-c, prostate-specific antigen [PSA] 10-20, or Gleason score 7). INTERVENTION: All patients received EBRT with >/=81Gy with or without neoadjuvant and concurrent androgen-deprivation therapy (ADT). OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Univariate and multivariate analyses were performed using a Cox proportional hazards model for PSA recurrence-free survival (PSA-RFS) and distant metastasis (DM). PCa-specific mortality (PCSM) was analyzed using a competing risk method. RESULTS AND LIMITATIONS: Median follow-up was 71 mo. Primary Gleason pattern 4 (hazard ratio [HR]: 3.26; p<0.0001), PPBC >/=50% (HR: 2.72; p=0.0007), and multiple IRFs (HR: 2.20; p=0.008) all were significant predictors of increased DM in multivariate
analyses. Primary Gleason pattern 4 (HR: 5.23; p<0.0001) and PPBC >/=50% (HR: 4.08; p=0.002) but not multiple IRFs (HR: 1.74; p=0.21) independently predicted for increased PCSM. Patients with UIR disease had inferior PSA-RFS (HR: 2.37; p<0.0001), DM (HR: 4.34; p=0.0003), and PCSM (HR: 7.39; p=0.007) compared with those with favorable intermediate-risk disease, despite being more likely to receive neoadjuvant ADT. Short follow-up and retrospective study design are the primary limitations. CONCLUSIONS: Intermediate-risk PCa is a heterogeneous collection of diseases that can be separated into favorable and unfavorable subsets. These groups likely will benefit from divergent therapeutic paradigms.

[29]

**TÍTULO / TITLE:** - Phase III, Randomized, Placebo-Controlled Study of Docetaxel in Combination With Zibotentan in Patients With Metastatic Castration-Resistant Prostate Cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


-●●Enlace al texto completo (gratuito o de pago) 1200/JCO.2012.46.4149

**AUTORES / AUTHORS:** - Fizazi KS; Higano CS; Nelson JB; Gleave M; Miller K; Morris T; Nathan FE; McIntosh S; Pemberton K; Moul JW

**INSTITUCIÓN / INSTITUTION:** - Department of Cancer Medicine, Institut Gustave Roussy, University of Paris Sud, 39 rue Camille Desmoulins, Villejuif 94805, France; fizazi@igr.fr.

**RESUMEN / SUMMARY:** - PURPOSE As part of the ENTHUSE (Endothelin A Use) program, the efficacy and safety of zibotentan (ZD4054), an oral specific endothelin A receptor antagonist, has been investigated in combination with docetaxel in patients with metastatic castration-resistant prostate cancer (CRPC). PATIENTS AND METHODS In this randomized, double-blind, placebo-controlled, phase III study, patients received intravenous docetaxel 75 mg/m(2) on day 1 of 21-day cycles plus oral zibotentan 10 mg or placebo once daily. The primary end point was overall survival (OS). Secondary end points included time to pain and prostate-specific antigen (PSA) progression, pain and PSA response, progression-free survival, health-related quality of life, and safety. Results A total of 1,052 patients received study treatment (docetaxel-zibotentan, n = 524; docetaxel-placebo, n = 528). At the time of data cutoff, there had been 277 and 280 deaths, respectively. There was no difference in OS for patients receiving docetaxel-zibotentan compared with those receiving docetaxel-placebo (hazard ratio, 1.00; 95% CI, 0.84 to 1.18; P = .963). No significant differences were observed on secondary end points, including time to pain progression (median 9.3 v 10.0 months, respectively) or pain response (odds ratio, 0.84; 95% CI, 0.61 to 1.16; P = .283). The median time to death
was 20.0 and 19.2 months for the zibotentan and placebo groups, respectively. The most commonly reported adverse events in zibotentan-treated patients were peripheral edema (52.7%), diarrhea (35.4%), alopecia (33.9%), and nausea (33.3%). CONCLUSION Docetaxel plus zibotentan 10 mg/d did not result in a significant improvement in OS compared with docetaxel plus placebo in patients with metastatic CRPC.

[30]

TITULO / TITLE: - Relationship between 6- and 9-month progression-free survival and overall survival in patients with metastatic urothelial cancer treated with first-line cisplatin-based chemotherapy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Galsky MD; Krege S; Lin CC; Hahn N; Ecke T; Moshier E; Sonpavde G; Godbold J; Oh WK; Bamias A

INSTITUCIÓN / INSTITUTION: - The Tisch Cancer Institute, Mount Sinai School of Medicine, New York, New York.

RESUMEN / SUMMARY: - BACKGROUND: Use of progression-free survival (PFS) as a clinical trial endpoint in first-line treatment of patients with metastatic urothelial carcinoma (UC) is attractive, but would be enhanced by establishing a correlation between PFS and overall survival (OS). METHODS: Data was pooled from 7 phase 2 and 3 trials evaluating cisplatin-based chemotherapy in metastatic UC. An independent cohort of patients enrolled on a phase 3 trial was used for external validation. Landmark analyses for progression at 6 and 9 months after treatment initiation were performed to minimize lead-time bias. A proportional hazards model was used to assess the utility of PFS for predicting OS. RESULTS: A total of 364 patients were included in the initial cohort. The median PFS was 8.21 months (95% confidence interval = 7.43, 8.39) and the median OS was 13.50 months (95% confidence interval = 11.80, 15.67). In the landmark analysis, the median OS for patients who progressed at 6 months was 3.87 months compared with 15.06 months for those patients who did not progress (P < .0001) and the median OS for patients who progressed at 9 months was 5.65 months compared with 21.39 months for those patients who did not progress (P < .0001). A Fleischer model demonstrated a statistically significant dependent correlation between PFS and OS. The findings were externally validated in an independent cohort. CONCLUSIONS: PFS at 6 and 9 months predicted OS in this analysis of patients with metastatic UC treated with first-line cisplatin-based chemotherapy and could potentially serve as endpoints in (randomized) phase 2 trials to screen the activity of novel regimens. Cancer 2013. © 2013 American Cancer Society.
[31] **TITULO / TITLE:** Punctuated evolution of prostate cancer genomes.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Baca SC; Prandi D; Lawrence MS; Mosquera JM; Romanel A; Drier Y; Park K; Kitabayashi N; Macdonald TY; Ghandi M; Van Allen E; Kryukov GV; Sboner A; Theurillat JP; Soong TD; Nickerson E; Auclair D; Tewari A; Beltran H; Onofrio RC; Boysen G; Guiducci C; Barbieri CE; Cibulskis K; Sivachenko A; Carter SL; Saksena G; Voet D; Ramos AH; Winckler W; Cipicchio M; Ardle K; Kantoff PW; Berger MF; Gabriel SB; Golub TR; Meyerson M; Lander ES; Elemento O; Getz G; Demichelis F; Rubin MA; Garraway LA

**INSTITUCIÓN / INSTITUTION:** Harvard Medical School, Boston, MA 02115, USA; The Broad Institute of Harvard and MIT, Cambridge, MA 02142, USA; Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA 02215, USA.

**RESUMEN / SUMMARY:** The analysis of exonic DNA from prostate cancers has identified recurrently mutated genes, but the spectrum of genome-wide alterations has not been profiled extensively in this disease. We sequenced the genomes of 57 prostate tumors and matched normal tissues to characterize somatic alterations and to study how they accumulate during oncogenesis and progression. By modeling the genesis of genomic rearrangements, we identified abundant DNA translocations and deletions that arise in a highly interdependent manner. This phenomenon, which we term “chromoplexy,” frequently accounts for the dysregulation of prostate cancer genes and appears to disrupt multiple cancer genes coordinately. Our modeling suggests that chromoplexy may induce considerable genomic derangement over relatively few events in prostate cancer and other neoplasms, supporting a model of punctuated cancer evolution. By characterizing the clonal hierarchy of genomic lesions in prostate tumors, we charted a path of oncogenic events along which chromoplexy may drive prostate carcinogenesis.


**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

BACKGROUND: Accurate estimation of life expectancy is essential to offering appropriate care to men with early-stage prostate cancer, but mortality risks associated with comorbidity are poorly defined. OBJECTIVE: To determine the effect of age, comorbidity, and tumor risk on other-cause and prostate cancer-specific mortality in men with early-stage disease. DESIGN: Prospective cohort study. SETTING: A nationally representative, population-based cohort. PATIENTS: 3183 men with nonmetastatic prostate cancer at diagnosis. MEASUREMENTS: Baseline self-reported comorbidity (scored as a count of 12 major comorbid conditions), tumor characteristics, initial treatment, and overall and disease-specific mortality through 14 years of follow-up. Survival analyses that accounted for competing risks were performed. RESULTS: Fourteen-year cumulative other-cause mortality rates were 24%, 33%, 46%, and 57% for men with 0, 1, 2, and 3 or more comorbid conditions, respectively. For men diagnosed at age 65 years, subhazard ratios for other-cause mortality among those with 1, 2, or 3 or more comorbid conditions (vs. none) were 1.2 (95% CI, 1.0 to 1.4), 1.7 (CI, 1.4 to 2.0), and 2.4 (CI, 2.0 to 2.8), respectively. Among men with 3 or more comorbid conditions, 10-year other-cause mortality rates were 26%, 40%, and 71% for those aged 60 years or younger, 61 to 74 years, and 75 years or older at diagnosis, respectively. Prostate cancer-specific mortality was minimal in patients with low-risk (3%) and intermediate-risk (7%) disease but appreciable in those with high-risk disease (18%) and did not vary by number of comorbid conditions (10% to 11% in all groups). LIMITATION: Comorbid conditions were self-reported. CONCLUSION: Older men with multiple major comorbid conditions are at high risk for other-cause mortality within 10 years of diagnosis and should consider this information when deciding between conservative management and aggressive treatment for low- or intermediate-risk prostate cancer. PRIMARY FUNDING SOURCE: National Cancer Institute.
INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, University of Athens, Panepistimiopolis, 15701 Athens, Greece.

RESUMEN / SUMMARY: - Background: Prostate cancer (PCa) is characterised by great heterogeneity of the disease progression rate. Tumours range from insignificant and not life threatening to high risk for relapse ones. Consequently, a large number of patients undergo unnecessary treatment. miR-145 is a well-documented tumour suppressor and its expression, which is regulated by the p53 pathway, has been found to be decreased in the majority of human malignancies. The aim of our study was to evaluate the clinical utility of miR-145 for the prognostication of PCa.

Methods: Total RNA was isolated from 137 prostate tissue specimens obtained from 73 radical prostatectomy-treated PCa patients and 64 transurethral- or open prostatectomy-treated benign prostate hyperplasia (BPH) patients. Following polyadenylation and reverse transcription, miR-145 levels were determined by quantitative real-time PCR assay, using SNORD48 (RNU48) for normalisation purposes.

Results: Downregulated miR-145 expression was found in PCa compared with BPH patients. The reduction of miR-145 expression in PCa was correlated with higher Gleason score, advanced clinical stage, larger tumour diameter and higher prostate-specific antigen (PSA) and follow-up PSA levels. In addition, higher risk for biochemical recurrence and significantly shorter disease-free survival (DFS) was found for the PCa patients expressing lower miR-145. Focusing on 'low- and intermediate-recurrence risk' PCa patients, miR-145 loss was revealed to be a reliable predictor of biochemical relapse and poor DFS independent from Gleason score, clinical stage, PSA and patients’ age.

Conclusion: The loss of the tumour-suppressor miR-145 increases the risk for disease progression and predicts the poor survival of PCa patients. British Journal of Cancer advance online publication 23 May 2013; doi:10.1038/bjc.2013.250 [www.bjcancer.com].

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TÍTULO / TITLE: - Prostate cancer-associated mutations in speckle-type POZ protein (SPOP) regulate steroid receptor coactivator 3 protein turnover.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 1073/pnas.1304502110

AUTORES / AUTHORS: - Geng C; He B; Xu L; Barbieri CE; Eedunuri VK; Chew SA; Zimmermann M; Bond R; Shou J; Li C; Blattner M; Lonard DM; Demichelis F; Coarfa C; Rubin MA; Zhou P; O’Malley BW; Mitsiades N

INSTITUCIÓN / INSTITUTION: - Departments of Medicine and Molecular and Cellular Biology and Center for Drug Discovery, Baylor College of Medicine, Houston, TX 77030.
The p160 steroid receptor coactivators (SRCs) SRC-1, SRC-2 [nuclear receptor coactivator (NCOA)2], and SRC-3 [amplified in breast cancer 1 (AIB1)/NCOA3] are key pleiotropic “master regulators” of transcription factor activity necessary for cancer cell proliferation, survival, metabolism, and metastasis. SRC overexpression and overactivation occur in numerous human cancers and are associated with poor clinical outcomes and resistance to therapy. In prostate cancer (PC), the p160 SRCs play critical roles in androgen receptor transcriptional activity, cell proliferation, and resistance to androgen deprivation therapy. We recently demonstrated that the E3 ubiquitin ligase adaptor speckle-type poxvirus and zinc finger (POZ) domain protein (SPOP) interacts directly with SRC-3 and promotes its cullin 3-dependent ubiquitination and proteolysis in breast cancer, thus functioning as a potential tumor suppressor. Interestingly, somatic heterozygous missense mutations in the SPOP substrate-binding cleft recently were identified in up to 15% of human PCs (making SPOP the gene most commonly affected by nonsynonymous point mutations in PC), but their contribution to PC pathophysiology remains unknown. We now report that PC-associated SPOP mutants cannot interact with SRC-3 protein or promote its ubiquitination and degradation. Our data suggest that wild-type SPOP plays a critical tumor suppressor role in PC cells, promoting the turnover of SRC-3 protein and suppressing androgen receptor transcriptional activity. This tumor suppressor effect is abrogated by the PC-associated SPOP mutations. These studies provide a possible explanation for the role of SPOP mutations in PC, and highlight the potential of SRC-3 as a therapeutic target in PC.

[35]

**Título / Title:** Re: monotherapy with tadalafil or tamsulosin similarly improved lower urinary tract symptoms suggestive of benign prostatic hyperplasia in an international, randomised, parallel, placebo-controlled clinical trial.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary


**Autores / Authors:** Kaplan SA

[36]

**Título / Title:** Clinical Progression, Acute Urinary Retention, Prostate-Related Surgeries, and Costs in Patients with Benign Prostatic Hyperplasia Taking Early Versus Delayed Combination 5alpha-Reductase Inhibitor Therapy and alpha-Blocker Therapy: A Retrospective Analysis.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Morlock R; Goodwin B; Gomez Rey G; Eaddy M

INSTITUCIÓN / INSTITUTION: - Optum, Eden Prairie, Minnesota. Electronic address: rmorlock@yourcarechoice.com.

RESUMEN / SUMMARY: - BACKGROUND: Two previous retrospective database analyses compared early combination therapy with an alpha-blocker (AB) and 5-alpha reductase inhibitor (5-ARI) to delayed combination therapy and found that patients receiving the delayed combination therapy were more likely to have clinical progression, acute urinary retention (AUR), and surgery. Although these studies indicate the clinical benefits of early treatment, both studies failed to take into account important baseline clinical measures, such as prostate-specific antigen (PSA) values. OBJECTIVE: This study was designed to compare clinical and cost differences in men with benign prostatic hyperplasia (BPH) who initiated early versus delayed combination therapy with a 5-ARI + an AB, factoring in baseline PSA values. METHODS: This retrospective claims data analysis assessed data from >14 million US men with linked medical data, pharmacy data, laboratory results, and enrollment information from January 1, 2000, to December 31, 2009. Men aged 50 or older and treated for BPH with a 5-ARI + an AB were identified. Patients were required to be eligible for services at least 6 months before and 12 months after the index medication date. Patients were assigned to 1 of 2 treatment groups based on therapy (early or delayed) and 3 cohorts based on availability of PSA laboratory values (patients with a PSA value, patients with a PSA value >1.5 and <10, and all patients). Using a logistic model, the likelihood of clinical progression (defined as the occurrence of AUR or prostate surgery) during the 12 months after the date of first prescription fill was compared between BPH patients receiving early versus delayed combination therapy. BPH-related medical costs (excluding pharmacy costs) were assessed using generalized linear models. RESULTS: Among the 13,551 patients identified for study inclusion, the highest risks for clinical progression, AUR, and prostate-related surgery were consistently demonstrated in patients with a PSA >1.5 and <10. Across all 3 cohorts, the delayed combination-treatment group was more likely to have clinical progression, AUR, and prostate-related surgeries versus the early combination-treatment group. The incremental difference in BPH-related costs between the delayed and early combination-treatment groups was $190 per patient overall; the greatest incremental difference ($397) was observed in patients with PSA >1.5 and <10.

CONCLUSION: The results suggest that early initiation of combination therapy with 5-ARI + an AB, compared with delayed initiation, can reduce the risks for clinical progression, AUR, and prostate-related surgeries, as well as BPH-related medical costs, in patients with BPH.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago)
1080/01621459.2012.665615
AUTORES / AUTHORS: - Almirall D; Lizotte DJ; Murphy SA
INSTITUCIÓN / INSTITUTION: - Faculty Research Fellow, Institute for Social Research, University of Michigan.

[38] TÍTULO / TITLE: - Clear Cell Papillary Renal Cell Carcinoma-like Tumors in Patients With Von Hippel-Lindau Disease Are Unrelated to Sporadic Clear Cell Papillary Renal Cell Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago)
1097/PAS.0b013e318282dab8
AUTORES / AUTHORS: - Williamson SR; Zhang S; Eble JN; Grignon DJ; Martignoni G; Brunelli M; Wang M; Gobbo S; Baldridge LA; Cheng L
INSTITUCIÓN / INSTITUTION: - Departments of *Pathology and Laboratory Medicine double daggerUrology, School of Medicine, Indiana University, Indianapolis, IN daggerDepartment of Pathology and Diagnostics, University of Verona, Verona, Italy.
RESUMEN / SUMMARY: - Clear cell papillary renal cell carcinoma (CCPRCC) shares morphologic overlap with clear cell renal cell carcinoma, although it lacks chromosome 3p and VHL gene abnormalities. Rare cases have been reported in von Hippel-Lindau (VHL) patients (germline mutation of the VHL gene), the significance of which is uncertain. We analyzed morphologic, immunohistochemical, and molecular features in 14 CCPRCC-like tumors and 13 clear cell renal cell carcinomas from 12 patients with VHL disease. Gross appearance of CCPRCC-like tumors ranged from yellow-orange to tan, red-brown, or extensively cystic. Histologic features included: small papillary tufts (79%), branched tubules (71%), branched papillae (64%), flattened peripheral cysts (64%), and apically aligned nuclei (43%). Almost all CCPRCC-like tumors (82%) lacked the characteristic immunoprofile of sporadic CCPRCC (CK7,
CAIX, CD10, AMACR), often showing diffuse CD10 labeling (64%), negative or focal CK7 reactivity (55%), or both (18%). Three tumors (27%) showed strong AMACR staining. Chromosome 3p deletion was often present (82%), similar to that observed in clear cell renal cell carcinomas (80%); no CCPRCC-like tumor had chromosome 7 or 17 abnormalities. In summary, tumors that histologically resemble CCPRCC sometimes occur in patients with VHL disease but usually lack the characteristic immunohistochemical and molecular profile, suggesting that they do not share the same pathogenesis.

[39]

TÍTULO / TITLE: - Low C4 gene copy numbers are associated with superior graft survival in patients transplanted with a deceased donor kidney.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Bay JT; Schejbel L; Madsen HO; Sorensen SS; Hansen JM; Garred P
INSTITUCIÓN / INSTITUTION: - Laboratory of Molecular Medicine, Department of Clinical Immunology, Rigshospitalet, Copenhagen, Denmark.
RESUMEN / SUMMARY: - Complement C4 is a central component of the classical and the lectin pathways of the complement system. The C4 protein exists as two isotypes C4A and C4B encoded by the C4A and C4B genes, both of which are found with varying copy numbers. Deposition of C4 has been implicated in kidney graft rejection, but a relationship between graft survival and serum C4 concentration as well as C4 genetic variation has not been established. We evaluated this using a prospective study design of 676 kidney transplant patients and 211 healthy individuals as controls. Increasing C4 gene copy numbers significantly correlated with the C4 serum concentration in both patients and controls. Patients with less than four total copies of C4 genes transplanted with a deceased donor kidney experienced a superior 5-year graft survival (hazard ratio 0.46, 95% confidence interval: 0.25-0.84). No significant association was observed in patients transplanted with a living donor. Thus, low C4 copy numbers are associated with increased kidney graft survival in patients receiving a kidney from a deceased donor. Hence, the degree of ischemia may influence the clinical impact of complement.Kidney International advance online publication, 29 May 2013; doi:10.1038/ki.2013.195.

[40]

TÍTULO / TITLE: - Patient Demographics, Quality of Life, and Disease Features of Men With Newly Diagnosed Prostate Cancer: Trends in the PSA Era.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
OBJETIVO: Describir cómo las características demográficas y diagnósticas de los hombres con cáncer de próstata en los Estados Unidos han cambiado desde 1999, usando datos del Registramiento Urológico Estratégico de Cáncer de la Próstata (CaPSURE). MÉTODOS: Los registros médicos de los pacientes inscritos en CaPSURE entre 1999 y 2011 se evaluaron. Se evaluaron las características demográficas, las características del diagnóstico, y el uso de los procedimientos de imagen. Se utilizó el cálculo de mantel-Haenszel para determinar las tendencias a lo largo de los años de diagnóstico. RESULTADOS: Entre 1999 y 2011, un total de 9572 pacientes fueron diagnosticados con cáncer de próstata y inscritos en CaPSURE en hospitales comunitarios (36), académicos (3), y de Veteranos (4). A lo largo del período de estudio, la edad media al diagnóstico se redujo, P <.01. En 2008-2011, se observó un incremento significativo en el diagnóstico de Gleason 7 o superior en comparación con 1999-2001 (50% vs 36%, P <.01), congruente con las modificaciones recientes del sistema de clasificación de la Gleason. También se observó un aumento significativo en el número medio de biopsias diagnósticas (13.3 vs 8.3, P <.01). Se observó una reducción significativa en el uso de cualquier modalidad de imagen (19% vs 45%, P <.01). Los promedios pretratamiento de la función urinaria y bowel no cambiaron, aunque hubo incrementos significativos en la función sexual observados en general (P <.01). CONCLUSIÓN: En los Estados Unidos, varios cambios en las características demográficas y diagnósticas de los hombres con nuevo diagnóstico de cáncer de próstata se observaron a lo largo de los últimos 12 años. La reducción de la utilización de la imagen y el aumento en el número de biopsias durante el diagnóstico de cáncer de próstata están en línea con las guías nacionales de urología sobre el diagnóstico y el manejo del cáncer de próstata.
OBJECTIVE: To explore the prognostic and predictive value of baseline variables in 512 patients with metastatic castration-resistant prostate cancer from the phase III Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) trial who were randomized to receive sipuleucel-T or control. METHODS: The most powerful of these prognostic factors, baseline prostate-specific antigen (PSA), was subdivided into quartiles to evaluate treatment effect patterns. Cox regression analyses were used to assess predictors of overall survival (OS) and sipuleucel-T treatment effect within PSA quartiles. Median OS was estimated by the Kaplan-Meier method. RESULTS: PSA was the strongest baseline prognostic factor (P <.0001). Furthermore, the sipuleucel-T treatment effect appeared greater with decreasing baseline PSA. The OS hazard ratio for patients in the lowest baseline PSA quartile (\leq 22.1 ng/mL) was 0.51 (95% confidence interval, 0.31-0.85) compared with 0.84 (95% confidence interval, 0.55-1.29) for patients in the highest PSA quartile (>134 ng/mL). Estimated improvement in median survival varied from 13.0 months in the lowest baseline PSA quartile to 2.8 months in the highest quartile. Estimated 3-year survival in the lowest PSA quartile was 62.6% for sipuleucel-T patients and 41.6% for control patients, representing a 50% relative increase. CONCLUSION: The greatest magnitude of benefit with sipuleucel-T treatment in this exploratory analysis was observed among patients with better baseline prognostic factors, particularly those with lower baseline PSA values. These findings suggest that patients with less advanced disease may benefit the most from sipuleucel-T treatment and provide a rationale for immunotherapy as an early treatment strategy in sequencing algorithms for metastatic castration-resistant prostate cancer.
INSTITUCIÓN / INSTITUTION: - Department of Urology, The Second Hunan Provincial People’s Hospital, Hunan Traditional Chinese Medical University, Changsha, Hunan Province, China.

RESUMEN / SUMMARY: - OBJECTIVE: To prospectively evaluate perioperative results and 12-month follow-up after plasmakinetic enucleation of the prostate (PKEP) and transvesical open prostatectomy (OP) for benign prostatic hyperplasia (BPH) >80 mL. METHODS: A total of 83 patients with a prostate >80 mL were randomized to either PKEP or OP. Perioperative and postoperative outcome data were obtained during a 12-month follow-up. RESULTS: No statistical differences were observed in the preoperative data. Both groups resulted in a similar and significant postoperative improvement in International Prostate Symptom Score (IPSS), quality of life (QOL), maximum uroflow rate (Qmax), postvoid residual (PVR) urine volume and prostate specific antigen (PSA), but no significant difference was found between the groups at the 12-month follow-up. Compared to OP, operation time (111.2 +/- 27.1 minutes vs 109.6 +/- 28.2 minutes, P = .708) were not significantly different between the groups, but blood loss was significantly less (10.2 +/- 4.5 g/l vs 15.1 +/- 4.3 g/l, P <.001), and bladder irrigation (2.4 +/- 1.0 days vs 4.3 +/- 1.1 days, P <.001), catheterization time (3.3 +/- 1.1 days vs 6.2 +/- 1.3 days, P <.001), and hospital stay (5.4 +/- 1.2 days vs 9.3 +/- 1.1 days, P <.001) were significantly shorter in the PKEP group. Effects on erectile function were similar in both groups, but adverse events were less frequent in the PKEP group. CONCLUSION: PKEP can be performed safely and is an equally effective procedure for treatment of large BPH with OP, with minimal complications and faster postoperative recovery. The PKEP helps to reduce the morbidity associated with OP and may become the attractive alternative to OP for patients with large BPH.

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[TÍTULO / TITLE:] Prospective Evaluation of Serum Sarcosine and Risk of Prostate Cancer in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial.

[RESUMEN / SUMMARY:] - Enlace al Resumen / Link to its Summary


[1093/carcin/bgt176]

[AUTORES / AUTHORS:] Koutros S; Meyer TE; Fox SD; Issaq HJ; Veenstra TD; Huang WY; Yu K; Albanes D; Chu LW; Andriole G; Hoover RN; Hsing AW; Berndt SI

[INSTITUCIÓN / INSTITUTION:] Division of Cancer Epidemiology and Genetics, National Cancer Institute. Rockville, MD.

[RESUMEN / SUMMARY:] Metabolomic profiling has identified, sarcosine, a derivative of the amino acid glycine, as an important metabolite involved in the
etiology or natural history of prostate cancer. We examined the association between serum sarcosine levels and risk of prostate cancer in 1,122 cases (813 non-aggressive and 309 aggressive) and 1,112 controls in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. Sarcosine was quantified using high-throughput liquid chromatography-mass spectrometry. A significantly increased risk of prostate cancer was observed with increasing levels of sarcosine (Odds Ratio (OR) for the highest quartile of exposure (Q4) versus the lowest quartile (Q1) = 1.30, 95% CI: 1.02, 1.65; P-trend 0.03). When stratified by disease aggressiveness, we observed a stronger association for nonaggressive cases (OR for Q4 vs Q1 = 1.44, 95% CI: 1.11, 1.88; P-trend 0.006) but no association for aggressive prostate cancer (OR for Q4 vs Q1 = 1.03, 95% CI: 0.73, 1.47; P-trend 0.89). Although not statistically significant, temporal analyses showed a stronger association between sarcosine and prostate cancer for serum collected closer to diagnosis, suggesting that sarcosine may be an early biomarker of disease. Interestingly, the association between sarcosine and prostate cancer risk was stronger among men with diabetes (OR= 2.66, 95% CI: 1.04, 6.84) compared to those without reported diabetes (OR=1.23, 95% CI: 0.95-1.59, p-interaction=0.01). This study found that elevated levels of serum sarcosine are associated with an increased prostate cancer risk and evidence to suggest that sarcosine may be an early biomarker for this disease.
externally using data from a randomized trial of the combination of methotrexate, vinblastine, doxorubicin plus cisplatin versus docetaxel plus cisplatin. RESULTS: The median survival of the development cohort was 13.8 months (95% confidence interval, 12.1 months-16.0 months); 68.2% of the patients had died at the time of last follow-up. On multivariable analysis, the number of visceral metastatic sites, Eastern Cooperative Oncology Group performance status, and leukocyte count were each found to be associated with overall survival (P < .05), whereas the site of the primary tumor and the presence of lymph node metastases were not. All 5 variables were included in the nomogram. When subjected to internal validation, the nomogram achieved a bootstrap-corrected concordance index of 0.626. When applied to the external validation cohort, the nomogram achieved a concordance index of 0.634. Calibration plots suggested that the nomogram was well calibrated for all predictions. CONCLUSIONS: Based on routinely measured pretreatment variables, a nomogram was constructed that predicts survival in patients with unresectable and/or metastatic urothelial cancer who are treated with cisplatin-based chemotherapy. This model may be useful in patient counseling and clinical trial design. Cancer 2013. © 2013 American Cancer Society.

[45]
TÍTULO / TITLE: - Radiotherapy with rectangular fields is associated with fewer clinical failures than conformal fields in the high-risk prostate cancer subgroup: Results from a randomized trial.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Heemsbergen WD; Al-Mamgani A; Witte MG; van Herk M; Lebesque JV

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands. Electronic address: w.heemsbergen@nki.nl.

RESUMEN / SUMMARY: - OBJECTIVE: High-risk prostate cancer patients are at risk for subclinical disease and micro-metastasis at the time of treatment. Nowadays, tight margins reduce dose to periprostatic areas compared to earlier techniques. We investigated whether rectangular fields were associated with fewer failures compared to conformal fields (with lower extraprostatic dose).

METHODS: We selected 164 high-risk patients from the trial population of 266 T1-T4N0M0 patients, randomized between rectangular (n=79) and conformal fields (n=85). Prescribed dose was 66Gy to the prostate and seminal vesicles plus 15mm margin. We compared clinical failure rates (in- and excluding local
failures), between both arms. Dose differences around the prostate were calculated based on an inter-patient mapping method. RESULTS: Median follow-up was 34 months. There were 9 clinical failures in the rectangular arm versus 24 in the conformal arm (p=0.012). Number of failures outside the prostate was 7 and 19, respectively (p=0.025). We observed average dose differences of 5-35 Gy between the arms in the regions around the prostate. CONCLUSIONS: We found a significantly lower risk of early tumor progression for patients treated with rectangular fields. Treatment failure can probably in part be prevented by irradiation of areas suspected of subclinical disease in high-risk prostate cancer.

[46] TÍTULO / TITLE: Vasohibin-1 is a new predictor of disease-free survival in operated patients with renal cell carcinoma.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Kanomata N; Sato Y; Miyaji Y; Nagai A; Moriya T
INSTITUCIÓN / INSTITUTION: Department of Pathology, Kawasaki Medical School, Kurashiki, Okayama, Japan.
RESUMEN / SUMMARY: BACKGROUND: Vasohibin-1 (VASH1) is an endothelium-produced angiogenesis inhibitor. Renal cell carcinoma is highly vascularised, but the significance of endogenous VASH1 in renal cell carcinoma has not been defined. AIMS: To identify VASH1 expression and its possible relationship with various clinicopathological factors and prognosis in renal cell carcinoma. METHODS: A retrospective analysis of 122 tumours obtained from 118 consecutive patients with renal cell carcinoma was performed. The expression patterns of VASH1, CD31, vascular endothelial growth factor (VEGF) and VEGF receptor type 2 (VEGFR2) were examined immunohistochemically and their relationships with clinicopathological factors were analysed. RESULTS: Microvessel density, VASH1 and VEGFR2 expression were significantly higher in clear cell carcinoma than in other subtypes. The VEGF expression pattern differed significantly between clear cell carcinoma and other histological subtypes. VASH1, pT factor and TNM stage were significantly associated with disease-free survival (p=0.030, p = 0.0012 and p = 0.0018, respectively). Cox models of multivariable disease-free survival analyses indicated that VASH1 and stage are independent prognostic factors (p=0.019 and p = 0.024). CONCLUSIONS: VASH1 expression may be useful for estimating the prognosis of renal cell carcinoma. Further studies of the role of VASH1 in renal cell carcinoma involving larger sample sizes are warranted.
TÍTULO / TITLE: - Axitinib versus sorafenib as second-line treatment for advanced renal cell carcinoma: overall survival analysis and updated results from a randomised phase 3 trial.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Motzer RJ; Escudier B; Tomczak P; Hutson TE; Michaelson MD; Negrier S; Oudard S; Gore ME; Tarazi J; Hariharan S; Chen C; Rosbrook B; Kim S; Rini BI

INSTITUCIÓN / INSTITUTION: - Memorial Sloan-Kettering Cancer Center, New York, NY, USA. Electronic address: motzerr@mskcc.org.

RESUMEN / SUMMARY: - BACKGROUND: In a phase 3 trial comparing the efficacy and safety of axitinib versus sorafenib as second-line treatment for metastatic renal cell carcinoma, patients given axitinib had a longer progression-free survival (PFS). Here, we report overall survival and updated efficacy, quality of life, and safety results. METHODS: Eligible patients had clear cell metastatic renal cell carcinoma, progressive disease after one approved systemic treatment, and an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0-1. 723 patients were stratified by ECOG PS and previous treatment and randomly allocated (1:1) to receive axitinib (5 mg twice daily; n=361) or sorafenib (400 mg twice daily; n=362). The primary endpoint was PFS assessed by a masked, independent radiology review committee. We assessed patient-reported outcomes using validated questionnaires. Baseline characteristics and development of hypertension on treatment were studied as prognostic factors. Efficacy was assessed in the intention-to-treat population, and safety was assessed in patients who received at least one dose of the study drug. This ongoing trial is registered on ClinicalTrials.gov, number NCT00678392. FINDINGS: Median overall survival was 20.1 months (95% CI 16.7-23.4) with axitinib and 19.2 months (17.5-22.3) with sorafenib (hazard ratio [HR] 0.969, 95% CI 0.800-1.174; one-sided p=0.3744). Median investigator-assessed PFS was 8.3 months (95% CI 6.7-9.2) with axitinib and 5.7 months (4.7-6.5) with sorafenib (HR 0.656, 95% CI 0.552-0.779; one-sided p<0.0001). Patient-reported outcomes scores were similar in the treatment groups at baseline, were maintained during treatment, but decreased at end-of-treatment. Common grade 3 or higher treatment-related adverse events were hypertension (60 [17%]), diarrhoea (40 [11%]), and fatigue (37 [10%]) in 359 axitinib-treated patients and hand-foot syndrome (61 [17%]), hypertension (43 [12%]), and diarrhoea (27 [8%]) in 355 sorafenib-treated patients. In a post-hoc 12-week landmark analysis, median overall survival was longer in patients with a
diastolic blood pressure of 90 mm Hg or greater than in those with a diastolic blood pressure of less than 90 mm Hg: 20.7 months (95% CI 18.4-24.6) versus 12.9 months (10.1-20.4) in the axitinib group (p=0.0116), and 20.2 months (17.1-32.0) versus 14.8 months (12.0-17.7) in the sorafenib group (one-sided p=0.0020). INTERPRETATION: Although overall survival, a secondary endpoint for the study, did not differ between the two groups, investigator-assessed PFS remained longer in the axitinib group compared with the sorafenib group. These results establish axitinib as a second-line treatment option for patients with metastatic renal cell carcinoma. FUNDING: Pfizer Inc.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Motzer RJ; Escudier B; Bukowski R; Rini BI; Hutson TE; Barrios CH; Lin X; Fly K; Matczak E; Gore ME
INSTITUCIÓN / INSTITUTION: Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, 10021 New York, NY, USA.
RESUMEN / SUMMARY: Background: Prognostic factors for progression-free survival (PFS), overall survival (OS), and long-term OS (>/=30 months) were investigated in sunitinib-treated patients with metastatic renal cell carcinoma (RCC). Methods: Data were pooled from 1059 patients in six trials. Baseline variables, including ethnicity, were analysed for prognostic significance by Cox proportional-hazards model. Results: Median PFS and OS were 9.7 and 23.4 months, respectively. Multivariate analysis of PFS and OS identified independent predictors, including ethnic origin, Eastern Cooperative Oncology Group performance status, time from diagnosis to treatment, prior cytokine use, haemoglobin, lactate dehydrogenase, corrected calcium, neutrophils, platelets, and bone metastases (OS only). Characteristics of long-term survivors (n=215, 20%) differed from those of non-long-term survivors; independent predictors of long-term OS included ethnic origin, bone metastases, and corrected calcium. There were no differences in PFS (10.5 vs 7.2 months; P=0.1006) or OS (23.8 vs 21.4 months; P=0.2135) in white vs Asian patients; however, there were significant differences in PFS (10.5 vs 5.7 months; P<0.001) and OS (23.8 vs 17.4 months; P=0.0319) in white vs non-white, non-Asian patients. Conclusion: These analyses identified risk factors to survival with sunitinib, including potential ethnic-based differences, and validated risk factors previously reported in advanced RCC. British Journal of Cancer advance online publication, 21 May 2013; doi:10.1038/bjc.2013.236 www.bjcancer.com.
TÍTULO / TITLE: - Circulating adipokine levels and endometrial cancer risk in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Luhn P; Dallal CM; Weiss J; Black A; Huang WY; Lacey JV; Hayes RB; Stanczyk FZ; Wentzensen N; Brinton LA

INSTITUCIÓN / INSTITUTION: - 1DCEG, National Cancer Institute.

RESUMEN / SUMMARY: - BACKGROUND: Circulating adipokine levels may be associated with endometrial cancer risk, yet few studies have evaluated these markers prospectively. METHODS: We conducted a nested case-control study of postmenopausal women in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (n=78,216), including 167 incident endometrial cancer cases and 327 controls that were matched on age, study center, race, study year of diagnosis, year of blood draw, time of day of blood draw and menopausal hormone therapy (MHT) use. Adipokine and estradiol levels were categorized into tertiles (T). Odds ratios (ORs) and 95% confidence intervals (CIs) for the associations of adiponectin, leptin and visfatin with endometrial cancer risk were estimated by conditional logistic regression, adjusting for known endometrial cancer risk factors, including body mass index (BMI) and circulating estradiol levels. RESULTS: Adiponectin levels were inversely associated with risk of endometrial cancer [OR T3vsT1=0.48 (95%CI: 0.29-0.80); p-trend<0.01], whereas elevated leptin levels showed a positive association [2.77 (1.60-4.79); p-trend<0.01]. These results remained significant after adjustment for estradiol, but not after further adjustment for BMI. When analyses were restricted to non-MHT users, associations of adiponectin and leptin were stronger and remained significant after adjustment for estradiol and BMI [0.27 (0.09-0.80); p-trend=0.01 and 4.29 (1.07-17.15); p-trend=0.02, respectively]. Non-significant positive associations were observed for visfatin. CONCLUSION: Adipokines may influence endometrial cancer risk through pathways other than estrogen-mediated cell growth in postmenopausal women not currently on MHT. Impact: Understanding how adipokines influence endometrial cancer risk may help to elucidate biological mechanisms important for the observed obesity-endometrial cancer association.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Nakabayashi M; Hayes J; Taplin ME; Lefebvre P;
Lafeuille MH; Pomerantz M; Sweeney C; Duh MS; Kantoff PW

INSTITUCIÓN / INSTITUTION: - Lank Center for Genitourinary Oncology, Dana-
Farber Cancer Institute and Harvard Medical School, Boston, Massachusetts.

RESUMEN / SUMMARY: - BACKGROUND: This study sought to characterize
Modern patients with castration-resistant prostate cancer (CRPC) and identify
pretreatment clinical predictors of survival. METHODS: A cohort of men with
CRPC with and without metastases (M) treated with secondary hormonal
therapy (2eHT) and/or chemotherapy (CT) was identified from the authors’
institutional database. Associations of patient and disease characteristics at
diagnosis, at androgen-deprivation therapy (ADT) initiation, at CRPC index
date, and survival were evaluated. CRPC index date was defined as the start
date of either 2eHT or CT, whichever came first. RESULTS: In the cohort of 622
men, 434 men (70%) had M-positive disease; 552 men (89%) received 2eHT
and 70 men (11%) received CT as their initial CRPC treatment. There were 410
deaths (66%) at the time of analysis. Median overall survival (OS) was 35
months (quartile 1, quartile 3: 21 months, 61 months). In multivariate analyses,
higher biopsy Gleason score, the presence of M at ADT initiation, shorter time
from ADT start to CRPC, higher prostate-specific antigen and poorer Eastern
Cooperative Oncology Group performance status at CRPC and M at CRPC
were predictive of shorter OS. Interestingly, whereas some men with biopsy
Gleason scores of 6 died of their disease (N = 42), they had a longer OS after
CRPC compared with those with a Gleason score >/= 7. CONCLUSIONS: This
large retrospective study of patients with CRPC in a tertiary cancer center
shows that biopsy Gleason score of 6 is associated with a less aggressive
CRPC course, and the impact that M at ADT initiation and CRPC have on

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TÍTULO / TITLE: - Paradoxical metastatic progression following 3months of neo-
adjuvant androgen suppression in the TROG 96.01 trial for men with locally
advanced prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Radiother Oncol. 2013 Apr 22. pii: S0167-

AUTORES / AUTHORS: - Denham JW; Steigler A; Tai KH; Joseph D; Matthews J;
Atkinson C; Spry NA; Turner S; North J; Christie D; Wynne C; Lamb DS
INSTITUCIÓN / INSTITUTION: - School of Medicine and Public Health, The University of Newcastle, Australia. Electronic address: Jim.Denham@newcastle.edu.au.

RESUMEN / SUMMARY: - PURPOSE: In the TROG 96.01 trial 6month neo-adjuvant androgen suppression (NAS) and radiotherapy (RT) for locally advanced prostate cancer prevented distant progressions (DPs) when compared to RT alone, but 3months did not. We ask why? METHODS: Between 1996 and 2000, 802 men with T2-4 N0 M0 prostate cancers received RT alone (0month NAS) to 66Gy, 3months or 6months NAS before RT. Interval hazards and cumulative incidences of DP were compared using competing risks methodology. RESULTS: In the first 4 follow-up years 39, 40 and 26 DPs were diagnosed in subjects treated with 0, 3 and 6month NAS, respectively. Compared with 0month, significant reductions in PSA doubling time in subjects with DP occurred following 3month NAS (p=0.01), but a significant reduction (p=0.01) and a near significant delay in DPs (p=0.06) occurred after 6month NAS. Subsequently 25, 20 and 11 DPs occurred in the three trial arms. After early secondary therapy for PSA or local progression 34, 19 and 12 DPs were diagnosed after median delays of almost 4years. CONCLUSIONS: The data are consistent with the failure of 3month NAS to prevent the progression of sub-clinical metastatic deposits already present before treatment.

[52]

TÍTULO / TITLE: - Prevalence of the metabolic syndrome and cardiovascular disease risk in chemotherapy-treated testicular germ cell tumour survivors.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Willemse PM; Burggraaf J; Hamdy NA; Weijl NI; Vossen CY; van Wulften L; van Steijn-van Tol AQ; Rosendaal FR; Osanto S

INSTITUCIÓN / INSTITUTION: - Department of Clinical Oncology, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands.

RESUMEN / SUMMARY: - Background: Testicular cancer patients have an increased risk for cardiovascular disease (CVD), which might be related to the increased prevalence of the metabolic syndrome (MetS) in this group of patients. Methods: We assessed the prevalence of MetS and calculated the 10-year CVD risk in a cohort of 255 testicular germ cell tumour survivors (median age, 38.7 years; interquartile range, 31-48) at a mean of 7.8 years after anticancer treatment, and compared these with data obtained from 360 healthy men. Results: Survivors had an age-adjusted increased risk for MetS of 1.9 compared with that of healthy controls. The risk for MetS was highest in survivors treated with combination chemotherapy (CT) 2.4 (Adult Treatment Panel of the National Cholesterol Education Program classification) and 2.2
The risk of MetS was especially increased in survivors with testosterone levels in the lowest quartile (OR, 2.5). Ten-year cardiovascular risk as assessed by the Framingham Risk Score (3.0%) and Systemic Coronary Risk Evaluation (1.7%) algorithms was low, independent of treatment, and was comparable to controls. Conclusion: Testicular germ cell tumour survivors have an increased prevalence of MetS, with hypogonadism and CT treatment being clear risk factors for the development of the syndrome. The increased prevalence of MetS was not associated with an increased 10-year cardiovascular risk. British Journal of Cancer advance online publication, 9 May 2013; doi:10.1038/bjc.2013.226 www.bjcancer.com.

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[53]

**TÍTULO / TITLE:** - Androgen-responsive long noncoding RNA CTBP1-AS promotes prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - EMBO J. 2013 May 3. doi: 10.1038/emboj.2013.99.

**AUTORES / AUTHORS:** - Takayama KI; Horie-Inoue K; Katayama S; Suzuki T; Tsutsumi S; Ikeda K; Urano T; Fujimura T; Takagi K; Takahashi S; Homma Y; Ouchi Y; Aburatani H; Hayashizaki Y; Inoue S

**INSTITUCIÓN / INSTITUTION:** - 1] Department of Anti-Aging Medicine, Graduate School of Medicine, University of Tokyo, Bunkyo-ku, Tokyo, Japan [2] Department of Geriatric Medicine, Graduate School of Medicine, University of Tokyo, Bunkyo-ku, Tokyo, Japan [3] Division of Gene Regulation and Signal Transduction, Research Center for Genomic Medicine, Saitama Medical University, Hidaka, Saitama, Japan.

**RESUMEN / SUMMARY:** - High-throughput techniques have identified numerous antisense (AS) transcripts and long non-coding RNAs (ncRNAs). However, their significance in cancer biology remains largely unknown. Here, we report an androgen-responsive long ncRNA, CTBP1-AS, located in the AS region of C-terminal binding protein 1 (CTBP1), which is a corepressor for androgen receptor. CTBP1-AS is predominantly localized in the nucleus and its expression is generally upregulated in prostate cancer. CTBP1-AS promotes both hormone-dependent and castration-resistant tumour growth. Mechanistically, CTBP1-AS directly represses CTBP1 expression by recruiting the RNA-binding transcriptional repressor PSF together with histone deacetylases. CTBP1-AS also exhibits global androgen-dependent functions by inhibiting tumour-suppressor genes via the PSF-dependent mechanism thus promoting cell cycle progression. Our findings provide new insights into the functions of ncRNAs that directly contribute to prostate cancer progression.
[54] TÍTULO / TITLE: - Is it time to reevaluate definitive therapy in prostate cancer?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1093/jnci/djt094
AUTORES / AUTHORS: - Madan RA; Shah AA; Dahut WL
INSTITUCIÓN / INSTITUTION: - Clinical Director, Center for Cancer Research, National Cancer Institute, National Institutes of Health, 10 Center Dr, Bethesda, MD 20892. dahutw@mail.nih.gov.

[55] TÍTULO / TITLE: - Germline BRCA Mutations Are Associated With Higher Risk of Nodal Involvement, Distant Metastasis, and Poor Survival Outcomes in Prostate Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1200/JCO.2012.43.1882
AUTORES / AUTHORS: - Castro E; Goh C; Olmos D; Saunders E; Leongamornlert D; Tymrakiewicz M; Mahmud N; Dadaev T; Govindasami K; Guy M; Sawyer E; Wilkinson R; Ardern-Jones A; Ellis S; Frost D; Peock S; Evans DG; Tischkowitz M; Cole T; Davidson R; Eccles D; Brewer C; Douglas F; Porteous ME; Donaldson A; Dorkins H; Izatt L; Cook J; Hodgson S; Kennedy MJ; Side LE; Eason J; Murray A; Antoniou AC; Easton DF; Kote-Jarai Z; Eeles R
INSTITUCIÓN / INSTITUTION: - Spanish National Cancer Research Centre 3, Melchor Fernandez Almagro, Madrid, 28029, España; dolmos@cnio.es.
RESUMEN / SUMMARY: - PURPOSE To analyze the baseline clinicopathologic characteristics of prostate tumors with germline BRCA1 and BRCA2 (BRCA1/2) mutations and the prognostic value of those mutations on prostate cancer (PCa) outcomes. PATIENTS AND METHODS This study analyzed the tumor features and outcomes of 2,019 patients with PCa (18 BRCA1 carriers, 61 BRCA2 carriers, and 1,940 noncarriers). The Kaplan-Meier method and Cox regression analysis were used to evaluate the associations between BRCA1/2 status and other PCa prognostic factors with overall survival (OS), cause-specific OS (CSS), CSS in localized PCa (CSS_M0), metastasis-free survival (MFS), and CSS from metastasis (CSS_M1). Results PCa with germline BRCA1/2 mutations were more frequently associated with Gleason >/= 8 (P = .00003), T3/T4 stage (P = .003), nodal involvement (P = .00005), and metastases at diagnosis (P = .005) than PCa in noncarriers. CSS was significantly longer in
noncarriers than in carriers (15.7 v 8.6 years, multivariable analyses [MVA] P = .015; hazard ratio [HR] = 1.8). For localized PCa, 5-year CSS and MFS were significantly higher in noncarriers (96% v 82%; MVA P = .01; HR = 2.6%; and 93% v 77%; MVA P = .009; HR = 2.7, respectively). Subgroup analyses confirmed the poor outcomes in BRCA2 patients, whereas the role of BRCA1 was not well defined due to the limited size and follow-up in this subgroup.

CONCLUSION Our results confirm that BRCA1/2 mutations confer a more aggressive PCa phenotype with a higher probability of nodal involvement and distant metastasis. BRCA mutations are associated with poor survival outcomes and this should be considered for tailoring clinical management of these patients.

[56]

TÍTULO / TITLE: Androgen deprivation therapy and the risk of colorectal cancer in patients with prostate cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Assayag J; Yin H; Benayoun S; Pollak MN; Suissa S; Azoulay L

INSTITUCIÓN / INSTITUTION: Centre for Clinical Epidemiology, Lady Davis Institute, Jewish General Hospital, 3755 Cote Sainte-Catherine, H425.1, Montreal, QC, H3T 1E2, Canada.

RESUMEN / SUMMARY: PURPOSE: Androgens are known to play an important protective role on colorectal carcinogenesis, and thus the objective of this study was to determine whether androgen deprivation therapy (ADT) is associated with an increased risk of incident colorectal cancer in patients with prostate cancer. METHODS: We conducted a population-based cohort study within the UK General Practice Research Database population which included all patients newly diagnosed with prostate cancer between 1 January 1988 and 31 December 2008, followed until 31 December 2009. Time-dependent Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of incident primary colorectal cancer associated with the use of ADT. Secondary analyses considered cumulative duration of use and specific ADTs. RESULTS: The cohort included a total of 21,503 patients, of whom 184 were diagnosed with colorectal cancer during a mean (SD) follow-up 4.0 (3.0) years (rate 2.4/1,000 person-years). Overall, use of ADT was not associated with an increased risk of colorectal cancer (HR 0.99, 95% CI 0.73-1.35). Similarly, no association was observed in terms of duration use, although this secondary analysis may have been limited by statistical power. With
respect to specific ADTs, bilateral orchiectomy was the only therapy associated with an increased risk of colorectal cancer (HR 2.50, 95 % CI 1.13-5.52).

CONCLUSION: Overall, the use of ADT is not associated with an increased risk of incident colorectal cancer. The increased risk observed with bilateral orchiectomy may possibly be due to the prolonged androgen suppression of this therapy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Joh HK; Giovannucci EL; Bertrand KA; Lim S; Cho E
INSTITUCIÓN / INSTITUTION: - Channing Division of Network Medicine, 181 Longwood Ave, Boston, MA 02115. eunyoung.cho@channing.harvard.edu.
RESUMEN / SUMMARY: - Background Although the kidney is a primary organ for vitamin D metabolism, the association between vitamin D and renal cell cancer (RCC) remains unclear. Methods We prospectively evaluated the association between predicted plasma 25-hydroxyvitamin D [25(OH)D] and RCC risk among 72 051 women and 46 380 men in the period from 1986 to 2008. Predicted plasma 25(OH)D scores were computed using validated regression models that included major determinants of vitamin D status (race, ultraviolet B flux, physical activity, body mass index, estimated vitamin D intake, alcohol consumption, and postmenopausal hormone use in women). Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using Cox proportional hazards models. All statistical tests were two-sided. Results During 22 years of follow-up, we documented 201 cases of incident RCC in women and 207 cases in men. The multivariable hazard ratios between extreme quintiles of predicted 25(OH)D score were 0.50 (95% CI = 0.32 to 0.80) in women, 0.59 (95% CI = 0.37 to 0.94) in men, and 0.54 (95% CI = 0.39 to 0.75; P trend < .001) in the pooled cohorts. An increment of 10ng/mL in predicted 25(OH)D score was associated with a 44% lower incidence of RCC (pooled HR = 0.56, 95% CI = 0.42 to 0.74). We found no statistically significant association between vitamin D intake estimated from food-frequency questionnaires and RCC incidence. Conclusion Higher predicted plasma 25(OH)D levels were associated with a statistically significantly lower risk of RCC in men and women. Our findings need to be confirmed by other prospective studies using valid markers of long-term vitamin D status.
Association between race and follow-up diagnostic care after a positive prostate cancer screening test in the Prostate, Lung, Colorectal, and Ovarian cancer screening trial.

BACKGROUND: Follow-through of a positive screening test is necessary to reap the potential benefits of cancer screening. Racial variation in follow-through diagnostic care may underlie a proportion of the known disparity in prostate cancer mortality. The authors used data from the screening arm of the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial to determine whether race is associated with the use of follow-up diagnostic testing after a positive initial screening evaluation. METHODS: Men who had a prostate-specific antigen (PSA) level >4 ng/mL at any time during the study were included. The proportion of men who underwent follow-up evaluation with a repeat PSA, a prostate biopsy, or either test within 9 months was determined, and the authors tested for differences in follow-through according to race using mixed-effects multivariate models with a random effect for accrual site to account for clustering. Models were stratified according to age (<65 years and ≥65 years). RESULTS: Among 6294 men who had a PSA elevation during the study period, 70% underwent a repeat PSA or prostate biopsy within 9 months. Non-Hispanic black men aged <65 years had 45% lower odds of undergoing a repeat PSA test or prostate biopsy compared with non-Hispanic white men (odds ratio, 0.55; 95% confidence interval, 0.37-0.82), whereas there was no racial difference in follow-through among older men. CONCLUSIONS: The current results suggest that limitations in access to care among non-Hispanic black men under the age of Medicare eligibility may underlie the paradoxically low use of follow-through diagnostic care among non-Hispanic black men in the United States. Cancer 2013;119:2223-2229. © 2013 American Cancer Society.

Pain questionnaire performance in advanced prostate cancer: comparative results from two international clinical trials.

BACKGROUND: Follow-through of a positive screening test is necessary to reap the potential benefits of cancer screening. Racial variation in follow-through diagnostic care may underlie a proportion of the known disparity in prostate cancer mortality. The authors used data from the screening arm of the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial to determine whether race is associated with the use of follow-up diagnostic testing after a positive initial screening evaluation. METHODS: Men who had a prostate-specific antigen (PSA) level >4 ng/mL at any time during the study were included. The proportion of men who underwent follow-up evaluation with a repeat PSA, a prostate biopsy, or either test within 9 months was determined, and the authors tested for differences in follow-through according to race using mixed-effects multivariate models with a random effect for accrual site to account for clustering. Models were stratified according to age (<65 years and ≥65 years). RESULTS: Among 6294 men who had a PSA elevation during the study period, 70% underwent a repeat PSA or prostate biopsy within 9 months. Non-Hispanic black men aged <65 years had 45% lower odds of undergoing a repeat PSA test or prostate biopsy compared with non-Hispanic white men (odds ratio, 0.55; 95% confidence interval, 0.37-0.82), whereas there was no racial difference in follow-through among older men. CONCLUSIONS: The current results suggest that limitations in access to care among non-Hispanic black men under the age of Medicare eligibility may underlie the paradoxically low use of follow-through diagnostic care among non-Hispanic black men in the United States. Cancer 2013;119:2223-2229. © 2013 American Cancer Society.
PURPOSE: To compare pain assessment questionnaires commonly used in advanced prostate cancer trials and to determine the psychometric characteristics and longitudinal relationships by contrasting questionnaire data from two international phase 2 trials. METHODS: Scores from the Present Pain Intensity (PPI) question of the McGill Pain Questionnaire, the pain intensity scale of the Brief Pain Inventory (BPI), and the Functional Assessment of Cancer Therapy-Prostate (FACT-P) were analyzed using Pearson correlation, intraclass correlation coefficient, and Cronbach’s alpha, respectively. Concordance was evaluated with Cohen’s kappa coefficient and McNemar test at baseline (n = 224) and two subsequent observations. RESULTS: PPI and FACT-P scores were associated with the BPI score at baseline for Trials 1 and 2: PPI r = 0.66 and 0.80, respectively (P < 0.001); FACT-P (pain scale) r = -0.76 and -0.82, respectively (P < 0.001). However, concordance analysis revealed that the BPI identified pain (score > 0) at higher rates than the PPI: at baseline, BPI: 89 % (64/72) and 77 % (95/124), PPI: 68 % (49/72) and 64 % (79/124) [Trials 1 and 2, respectively; McNemar test (P < 0.001) for both studies]. The FACT-P pain scale identified pain similarly to the BPI pain intensity scale; longitudinal analysis produced comparable findings. All pain scales met standard psychometric acceptability criteria, but the BPI and FACT-P performed better than the PPI. CONCLUSIONS: Data suggest the BPI pain intensity and FACT-P pain scales are better than the PPI question at capturing the pain experience among patients with advanced prostate cancer. Additional comparative research is needed in larger population samples.

[60]

TÍTULO / TITLE: Operative Safety and Oncologic Outcome of Laparoscopic Radical Nephrectomy for Renal Cell Carcinoma >7 cm: A Multicenter Study of 222 Patients.


AUTORES / AUTHORS: Luciani LG; Porpiglia F; Cai T; D'Elia C; Vattovani V; Giusti G; Tiscione D; Chiodini S; Peschechera R; Fiori C; Spina R; Parma P; Celia A; Malossini G
OBJECTIVE: To evaluate the safety of laparoscopic radical nephrectomy (LRN) for renal cell carcinoma (RCC) >7 cm, addressing the issue of modality and risk factors for complications and open conversion, and to assess the oncologic outcome. METHODS: The data of 222 patients undergoing LRN for RCC >7 cm prospectively enrolled from 2002 to 2010 at 5 urologic centers were reviewed. Transperitoneal LRN was performed by 5 experienced laparoscopic surgeons. The Clavien-Dindo classification was used to assess complications. Multivariable analysis of factors predictive of conversions was performed. Oncologic outcomes for survival were estimated using the Kaplan-Meier method. RESULTS: Median tumor size was 8.5 cm, operative time was 180 minutes, and blood loss was 280 mL. Forty-two patients (19%) received a blood transfusion. Six (2.7%) patients had grade III-IV complications: 2 with postoperative bleeding requiring abdominal re-exploration and 1 each with adrenal injury, splenic injury, wound diastasis, and respiratory insufficiency. Twelve patients (5.4%) were converted to open surgery. The diameter was 11.9 in converted groups and 8.5 cm in nonconverted groups (P = .001). Multivariable analysis revealed that pathologic stage was the only independent predictor of conversion (P = .002). The 5-year overall (OS), cancer-specific (CSS), and progression-free (PFS) survival was 74%, 78%, and 66%, respectively. The 5-year stage-adjusted CSS was 89% in pT2 and 40% in pT3 patients (P <.0001). Limitations of this study were its retrospective nature and the relatively short follow-up period for oncologic outcome. CONCLUSION: LRN for large RCC is a safe operation. Stage pT3 is a risk factor for open conversion and is associated to significantly lower cancer-specific survival compared with pT2 stage.

[61]

Metastatic non-clear cell renal cell carcinoma treated with targeted therapy agents: Characterization of survival outcome and application of the international mRCC database consortium criteria.

Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 1002/cncr.28151

Kroeger N; Xie W; Lee JL; Bjarnason GA; Knox JJ; Mackenzie MJ; Wood L; Srinivas S; Vaishamayan UN; Rha SY; Pal SK; Yuasa T; Donskov F; Agarwal N; Kollmannsberger CK; Tan MH; North SA; Rini BI; Choueiri TK; Heng DY

Tom Baker Cancer Center, Calgary, Alberta, Canada; University Medicine Greifswald, Department of Urology, Germany.
RESUMEN / SUMMARY: - BACKGROUND: This study aimed to apply the International mRCC Database Consortium (IMDC) prognostic model in metastatic non-clear cell renal cell carcinoma (nccRCC). In addition, the survival outcome of metastatic nccRCC patients was characterized. METHODS: Data on 2215 patients (1963 with clear-cell RCC [ccRCC] and 252 with nccRCC) treated with first-line VEGF- and mTOR-targeted therapies were collected from the IMDC. Time to treatment failure (TTF) and overall survival (OS) were compared in groups with favorable, intermediate, and poor prognoses according to IMDC prognostic criteria RESULTS: The median OS of the entire cohort was 20.9 months. nccRCC patients were younger (P < .0001) and more often presented with low hemoglobin (P = .014) and elevated neutrophils (P = .0001), but otherwise had clinicopathological features similar to those of ccRCC patients. OS (12.8 vs 22.3 months; P < .0001) and TTF (4.2 vs 7.8 months; P < .0001) were worse in nccRCC patients compared with ccRCC patients. The hazard ratio for death and TTF when adjusted for the prognostic factors was 1.41 (95% CI, 1.19-1.67; P < .0001) and 1.54 (95% CI, 1.33-1.79; P < .0001), respectively. The IMDC prognostic model reliably discriminated 3 risk groups to predict OS and TTF in nccRCC; the median OS of the favorable, intermediate, and poor prognostic groups was 31.4, 16.1, and 5.1 months, respectively (P < .0001), and the median TTF was 9.6, 4.9, and 2.1 months, respectively (P < .0001). CONCLUSIONS: Although targeted agents have significantly improved the outcome of patients with nccRCC, for the majority survival is still inferior compared with patients with ccRCC. The IMDC prognostic model reliably predicts OS and TTF in nccRCC and ccRCC patients. Cancer 2013. © 2013 American Cancer Society.

[62]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Sciarra A; Abrahamsson PA; Brausi M; Crook J; Galsky M; Klotz L; Mottet N; Sartor O; Tammela TL; Calais da Silva F
INSTITUCIÓN / INSTITUTION: - Department of Urology, University Sapienza, Rome, Italy. Electronic address: sciarra.md@libero.it.
RESUMEN / SUMMARY: - CONTEXT: Intermittent androgen deprivation (IAD) in prostate cancer (PCa) patients has been proposed to delay development of castration resistance and to reduce the side effects and costs of androgen deprivation therapy (ADT). OBJECTIVE: This review analyzes (1) the oncologic
and quality of life (QoL) results from randomized phase 3 trials comparing IAD and continuous ADT and (2) the prognostic parameters for IAD. EVIDENCE ACQUISITION: We searched the Medline and Cochrane Library databases (primary fields: prostate neoplasm and intermittent androgen deprivation; secondary fields: randomized trials, survival, quality of life, predictors) without language restriction. EVIDENCE SYNTHESIS: We found seven extensively described phase 3 trials randomizing 4675 patients to IAD versus continuous ADT. Other randomized trials investigating IAD have been performed, but available data are limited and have been published only in preliminary fashion. In all seven trials, patients spent most of their time on, rather than off, ADT. The induction periods ranged from 3 mo to 8 mo; in all but one trial, the PSA level designated for ADT discontinuation was <4 ng/ml. Mean follow-up ranged from 40-108 mo. Collectively, these trials support the concept that, mainly in metastatic cases, IAD can produce oncologic results similar to continuous ADT. In terms of overall survival, the hazard ratios for IAD and continuous ADT were very similar (range: 0.98-1.08). The QoL benefit of IAD appears to be modest at best. With IAD, QoL is likely influenced by the duration of the off-treatment periods and by the rate of testosterone recovery. CONCLUSIONS: The evidence indicates that IAD is not inferior to continuous ADT. Data are insufficient to determine whether IAD is able to prevent the long-term complications of ADT. More comparative analysis focused on QoL is warranted.

[63] TÍTULO / TITLE: - Stress response protein RBM3 attenuates the stem-like properties of prostate cancer cells by interfering with CD44 variant splicing.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Zeng Y; Wodzenski D; Gao D; Shiraishi T; Terada N; Li Y; Vander Griend DJ; Luo J; Kong C; Getzenberg RH; Kulkarni P
INSTITUCIÓN / INSTITUTION: - Urology, Institute of Urology, The First Hospital of China Medical University.
RESUMEN / SUMMARY: - Stress response pathways play an important role in cancer. The cold-inducible RNA-binding protein RBM3 is upregulated in several types of cancer including prostate cancer (PCa), but its pathogenic contributions are undetermined. RBM3 is expressed at low basal levels in human fetal prostate or in CD133+ prostate epithelial cells (PrEC), compared to the adult prostate or to CD133- PrEC, and RBM3 is downregulated in cells cultured in soft agar or exposed to stress. Notably, RBM3 overexpression in prostate cancer cells attenuated their stem cell-like properties in vitro as well as their tumorigenic potential in vivo. Interestingly, either overexpressing RBM3 or
culturing cells at 32 masculineC suppressed RNA splicing of the CD44 variant v8-v10 and increased expression of the standard CD44 (CD44s) isoform. Conversely, silencing RBM3 or culturing cells in soft agar (under conditions that enrich for stem cell-like cells) increased the ratio of CD44v8-v10 to CD44s mRNA. Mechanistic investigations showed that elevating CD44v8-v10 interfered with MMP9-mediated cleavage of CD44s and suppressed expression of cyclin D1, whereas siRNA-mediated silencing CD44v8-v10 impaired the ability of prostate cancer cells to form colonies in soft agar. Together these findings suggested that RBM3 contributed to stem cell-like character in prostate cancer by inhibiting CD44v8-v10 splicing. Our work uncovers a hitherto unappreciated role of RBM3 in linking stress-regulated RNA splicing to tumorigenesis, with potential prognostic and therapeutic implications in prostate cancer.

[64]

**TITULO / TITLE:** Increased chemo-sensitivity via targeting testicular nuclear receptor 4 (TR4)-Oct4-interleukin 1 receptor antagonist (IL1Ra) axis in prostate cancer CD133+ stem/progenitor cells to battle prostate cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** J Biol Chem. 2013 Apr 22.

**AUTORES / AUTHORS:** Yang DR; Ding XF; Luo J; Shan YX; Wang R; Lin SJ; Li G; Huang CK; Zhu J; Chen Y; Lee SO; Chang C

**INSTITUCIÓN / INSTITUTION:** University of Rochester Medical Center, United States;

**RESUMEN / SUMMARY:** Prostate cancer (PCa) stem/progenitor cells are known to have higher chemo-resistance than non-stem/progenitor cells, but the underlying molecular mechanism remains unclear. We found the expression of testicular nuclear receptor 4 (TR4) is significantly higher in PCa CD133+ stem/progenitor cells compared to CD133- non-stem/progenitor cells. Knocking down of TR4 levels in the established PCa stem/progenitor cells (PCSCs) and the CD133+ population of the C4-2 PCa cell line with lentiviral TR4-siRNA led to increased drug sensitivity to the two commonly used chemotherapeutic drugs, docetaxel and etoposide, judging from significantly reduced IC50 values and increased apoptosis in the TR4 knocked down cells. Mechanism dissection studies found that suppression of TR4 in these stem/progenitor cells led to down-regulation of Oct4 expression, which in turn, down-regulated the IL-1 receptor antagonist (IL1Ra) expression. Neutralization experiments via adding these molecules into the TR4 knocked-down PCa stem/progenitor cells reversed the chemo-resistance, suggesting that the TR4-Oct4-IL1Ra axis may play a critical role in the development of chemo-resistance in the PCa stem/progenitor cells. Together, these studies suggest that targeting TR4 may alter chemo-resistance of PCa stem/progenitor cells and this finding provides
the possibility of targeting TR4 as a new and better approach to overcome the chemo-resistance problem in PCa therapeutics.

[65]

**TÍTULO / TITLE:** A phase I study of folate immune therapy (EC90 vaccine administered with GPI-0100 adjuvant followed by EC17) in patients with renal cell carcinoma.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


- Enlace al texto completo (gratuito o de pago) 1097/CJI.0b013e3182917f59

**AUTORES / AUTHORS:** Amato RJ; Shetty A; Lu Y; Ellis R; Low PS

**INSTITUCIÓN / INSTITUTION:** Department of Internal Medicine, Memorial Hermann Cancer Center, Division of Oncology, University of Texas Health Science Center at Houston, Medical School, Houston, TX 77030, USA. robert.amato@uth.tmc.edu

**RESUMEN / SUMMARY:** This is the first phase I, open-label study to assess the safety, pharmacokinetics, and antitumor activity of a novel immunotherapeutic regimen known as Folate Immune (EC90 vaccine administered with GPI-0100 adjuvant followed by EC17, a folate-targeted hapten immunotherapy that targets folate receptor expressing cancer cells), which is designed to convert poorly immunogenic tumors to highly immunogenic tumors in patients with metastatic renal cell carcinoma. Three to 6 patients were enrolled in each cohort. In the vaccination phase, patients were given once weekly vaccinations of 0.2 mg of EC90 plus 3.0 mg of GPI-0100 for 3-5 weeks. In the treatment phase, patients were treated with 0.031, 0.092, or 0.276 mg/kg of EC17, 5 d/wk, for weeks 3, 4, or 6. Forty-one patients were enrolled in the study of which 33 patients received >/=1 treatment of EC17. Two dose-limiting toxicities were observed including grade 4 anaphylaxis and grade 3 pancreatitis. During the vaccination phase, mild to moderate injection site reactions were the most frequently reported adverse events. During the treatment phase, transient hypersensitivity reactions were the most common adverse event. Partial response was noted in 4% (1/28) of patients, and stable disease was noted in 54% (15/28) of patients after cycle 1 and was maintained in the majority of patients entering the extension phase of the study. EC90 vaccine with GPI-0100 adjuvant followed by EC17 is safe and well tolerated. The recommended regimen for further studies is 4 weekly vaccinations with 0.2 mg of EC90 plus 3.0 mg GPI-0100 followed by treatment with 0.3 mg of EC17.

[66]
PÁGINAS 53

TÍTULO / TITLE: - Time for a revision on the role of PSA response rate as a surrogate marker for median overall survival in docetaxel-based first-line treatment for patients with metastatic hormone-refractory prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


••Enlace al texto completo (gratuito o de pago) 5301/jbm.5000019

AUTORES / AUTHORS: - Roviello G; Petrioli R; Francini E

INSTITUCIÓN / INSTITUTION: - Medical Oncology Unit, University of Siena, Siena - Italy.

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[67]

TÍTULO / TITLE: - Evaluation of extraprostatic disease in the staging of prostate cancer by F-18 choline PET/CT: can PSA and PSA density help in patient selection?

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


••Enlace al texto completo (gratuito o de pago) 1097/MNM.0b013e3283620d5e

AUTORES / AUTHORS: - Calabria F; Chiaravalloti A; Tavolozza M; Ragano-Caracciolo C; Schillaci O

INSTITUCIÓN / INSTITUTION: - aDepartment of Nuclear Medicine and Molecular Imaging, INM IRCCS Neuromed, Pozzilli bDepartment of Biopathology and Diagnostic Imaging, University “Tor Vergata”, Rome, Italy.

RESUMEN / SUMMARY: - OBJECTIVE: The aim of our study was to evaluate the accuracy of F-18 choline positron emission tomography/computed tomography (PET/CT) in assessing the presence of extraprostatic disease during staging of prostate cancer, in relation to prostate-specific antigen (PSA) and PSA density, a PSA derivative that is useful for improving risk stratification in prostate cancer patients. METHODS: F-18 choline PET/CT was performed in 45 patients for early staging of biopsy-proven prostate cancer. None of the examined patients had received therapy before the examination. In all of them a transrectal ultrasonography had been performed earlier to calculate the prostate volume and PSA density. The mean PSA value was 25.5 (+/-38.1) ng/ml, whereas the mean PSA density was 0.70 (+/-0.88). RESULTS: Results of F-18 choline PET/CT were related to PSA and PSA density. PET/CT was positive for extraprostatic disease in 18/45 patients (40%) (mean PSA and PSA density were, respectively, 44.08 ng/ml and 1.08); PET/CT was negative for extraprostatic disease in 27/45 patients (60%) (mean PSA and PSA density were, respectively, 13.12 ng/ml and 0.4). PET/CT was positive in 13/18 patients (72%) with a PSA cutoff value greater than or equal to 18 ng/ml and in 5/21 (24%) with a PSA value less than 18 ng/ml (P=0.0017). PET/CT was positive in
16/18 patients (89%) with PSA density greater than or equal to 0.31 and in 2/18 (11%) with PSA density lower than 0.31 (P=0.0234). CONCLUSION: The possibility of detecting extraprostatic disease of prostate cancer with F-18 choline PET/CT is related to PSA and PSA density. In particular, F-18 choline PET/CT should be recommended only in patients with a PSA value of at least 18 ng/ml, whereas a PSA density of at least 0.31 ng/ml is more probably associated with distant metastases.
bone metastasis. The sensitivity of the (18)F-FCH PET was significantly higher (P = 0.001) in patients with ongoing ADT (85%; confidence interval, 80%-91%) than in patients without ADT (59.5%; confidence interval, 50%-69%). (18)F-FCH PET sensitivity was 77.5%, 80.7%, 85.2%, and 92.8% for the trigger PSA levels of more than 0.5, 1.0, 2.0, and 4.0 ng/mL, respectively. Scan sensitivity was 33% in patients with a trigger PSA level of less than 0.3 ng/mL and 77% in patients with a trigger PSA level of greater than 0.3 ng/mL, respectively (P = 0.001). Using a binary logistic regression analysis model, we showed trigger PSA and ADT to be the only significant predictors of positive PET findings.

CONCLUSION: (18)F-FCH PET/CT proved its potential as a noninvasive 1-stop diagnostic modality enabling us to correctly detect occult disease in 74% of patients and to differentiate localized from systemic disease. In patients with biochemical recurrence, it also guides to an optimal treatment approach after initial treatment. Trigger PSA and ADT are the 2 significant predictors of (18)F-FCH-positive PET lesions. ADT seems not to impair (18)F-FCH uptake in hormone-refractory prostate cancer patients.

[69]
TÍTULO / TITLE: - Re: Proton vs Intensity-Modulated Radiotherapy for Prostate Cancer: Patterns of Care and Early Toxicity.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

[70]
TÍTULO / TITLE: - Clinical activity of sorafenib in a previously treated advanced urothelial cancer patient.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Shah CH; Viktorsson K; Sherif A; Kanter L; Gryback P; Lewensohn R; Sandstrom P; Nilsson S; Ullen A
INSTITUCIÓN / INSTITUTION: - aDepartment of Oncology, Radiumhemmet Department of bUrology cPathology dRadiology, Karolinska University Hospital
A male patient, with advanced urothelial carcinoma, who had previously received cisplatin, was treated with sorafenib off-licence for 10.7 months. Evaluation of tumour response with computed tomography scans indicated a reduction in tumour size and necrosis of the metastases within 2 months. Progression-free survival was 10.5 months. Side effects were manageable and not beyond the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 grade 2. Molecular profiling of two of the proposed targets of sorafenib, platelet-derived growth factor receptor beta and vascular endothelial growth factor receptor 2, of the patient’s tumour lesion showed high and intermediate expression levels in the tumour as compared with the surrounding non-neoplastic tissue. In contrast to previous reports, we report a clinically meaningful effect of sorafenib in a patient with advanced urothelial carcinoma. Hence, it appears that a fraction of patients with this disease are sensitive to this compound. To identify subpopulations of responders, we propose that clinical trials evaluating sorafenib and other targeted drugs should be biomarker-driven and designed with endpoints that consider the mode of action of the specific compound.

[71]
TITULO / TITLE: - Sunitinib Plus Androgen Deprivation and Radiation Therapy for Patients With Localized High-Risk Prostate Cancer: Results From a Multinstitutional Phase 1 Study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
- Enlace al texto completo (gratuito o de pago)
1016/j.ijrobp.2012.12.029
AUTORES / AUTHORS: - Corn PG; Song DY; Heath E; Maier J; Meyn R; Kuban D; Depetrillo TA; Mathew P
INSTITUCIÓN / INSTITUTION: - Department of Genitourinary Medical Oncology, University of Texas M. D. Anderson Cancer Center, Houston, Texas. Electronic address: pcorn@mdanderson.org.
RESUMEN / SUMMARY: - PURPOSE: To evaluate the feasibility of administering sunitinib in combination with androgen deprivation therapy and external-beam intensity modulated radiation therapy (XRT) in patients with localized high-risk prostate cancer. METHODS AND MATERIALS: Seventeen men with localized adenocarcinoma of the prostate with cT2c-T4 or Gleason 8-10 or prostate-specific antigen >20 ng/mL received initial androgen deprivation (leuprolide 22.5 mg every 12 weeks plus oral bicalutamide 50 mg daily) for 4-8 weeks before oral sunitinib 12.5, 25, or 37.5 mg daily for 4 weeks as lead-in, then
concurrently with and 4 weeks after XRT (75.6 Gy in 42 fractions to prostate and seminal vesicles). A 3+3 sequential dose-escalation design was used to assess the frequency of dose-limiting toxicity (DLT) and establish a maximal tolerated dose of sunitinib. RESULTS: Sunitinib at 12.5- and 25-mg dose levels was well tolerated. The first 4 patients enrolled at 37.5 mg experienced a DLT during lead-in, and a drug interaction between sunitinib and bicalutamide was suspected. The protocol was revised and concurrent bicalutamide omitted. Of the next 3 patients enrolled at 37.5 mg, 2 of 3 receiving concurrent therapy experienced DLTs during radiation: grade 3 diarrhea and grade 3 proctitis, respectively. Only 1 of 7 patients completed sunitinib at 37.5 mg daily, whereas 3 of 3 patients (25 mg as starting dose) and 3 of 4 patients (25 mg as reduced dose) completed therapy. CONCLUSIONS: The feasibility of combined vascular endothelial growth factor receptor (VEGFR)/platelet-derived growth factor receptor (PDGFR) inhibitor therapy, androgen deprivation, and radiation therapy for prostate cancer was established. Using a daily dosing regimen with lead-in, concurrent, and post-XRT therapy, the recommended phase 2 dose of sunitinib is 25 mg daily.

[72]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i16.2466
AUTORES / AUTHORS: - Lee CH; Hsieh SY; Lin JL; Liu MS; Yen TH
INSTITUCIÓN / INSTITUTION: - Chern-Horng Lee, Sen-Yung Hsieh, Ja-Liang Lin, Maw-Sen Liu, Tzung-Hai Yen, College of Medicine, Chang Gung University, Taoyuan 333, Taiwan.
RESUMEN / SUMMARY: - AIM: To investigate outcomes of hepatocellular carcinomas (HCCs) in patients with chronic kidney disease (CKD). METHODS: Four hundred and forty patients referred between 2000 and 2002 for management of HCCs were categorized according to their CKD stage, i.e., estimated glomerular filtration rate (eGFR) > 90 (stage 1), 60-90 (stage 2), 30-60 (stage 3), 15-30 (stage 4), and < 15 (stage 5) mL/min per 1.73 m(2), respectively. Demographic, clinical and laboratory data were collected and mortality rates and cause of mortality were analyzed. The mortality data were examined with Kaplan-meier method and the significance was tested using a log-rank test. An initial univariate Cox regression analysis was performed to compare the frequency of possible risk factors associated with mortality. To control for possible confounding factors, a multivariate Cox regression analysis (stepwise backward approach) was performed to analyze those factors that
were significant in univariate models (P < 0.05) and met the assumptions of a proportional hazard model. RESULTS: Most HCC patients with CKD were elderly, with mean age of diagnosis of 60.6 +/- 11.9 years, and mostly male (74.8%). Hepatitis B, C and B and C co-infection virus were positive in 61.6%, 45.7% and 14.1% of the patients, respectively. It was found that patients with stages 4 and 5 CKD were not only older (P = 0.001), but also had higher hepatitis C virus carrier rate (P = 0.001), lower serum albumin level (P = 0.001), lower platelet count (P = 0.037), longer prothrombin time (P = 0.001) as well as higher proportions of advanced cirrhosis (P = 0.002) and HCCs (P = 0.001) than patients with stages 1 and 2 CKD. At the end of analysis, 162 (36.9%) patients had died. Kaplan-Meier analysis revealed that patients with stages 4 and 5 CKD suffered lower cumulative survival than stages 1 and 2 CKD (log-rank test, chi(2) = 11.764, P = 0.003). In a multivariate Cox-regression model, it was confirmed that CKD stage [odds ratio (OR) = 1.988, 95%CI: 1.012-3.906, P = 0.046], liver cirrhosis stage (OR = 3.571, 95%CI: 1.590-8.000, P = 0.002) and serum albumin level (OR = 0.657, 95%CI: 0.491-0.878, P = 0.005) were significant predictors for mortality in this population. CONCLUSION: HCC patients with stages 4 and 5 CKD had inferior survival than stages 1 and 2 CKD. This warrants further studies.

[73] TITULO / TITLE: - Toxicities Following Treatment with Bisphosphonates and Receptor Activator of Nuclear Factor-kappaB Ligand Inhibitors in Patients with Advanced Prostate Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Gartrell BA; Coleman RE; Fizazi K; Miller K; Saad F; Sternberg CN; Galsky MD

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA.
Electronic address: bgartrel@montefiore.org.
RESUMEN / SUMMARY: - CONTEXT: Advanced prostate cancer (PCA) is associated with skeletal complications, both as a result of bone metastases and because of fractures associated with fragility due to androgen-deprivation therapy (ADT). Osteoclast inhibitors are commonly used to reduce skeletal complications but are associated with a number of potential adverse events. OBJECTIVE: To review clinical trials of osteoclast inhibitors in advanced PCAs, to discuss the adverse event profile of these agents, and to discuss strategies to address specific adverse events. EVIDENCE ACQUISITION: PubMed was
searched for reports of clinical trials of osteoclast inhibitors in advanced PCa. As zoledronic acid and denosumab are used most commonly in this disease, these trials were the focus. The literature was reviewed to identify key publications addressing the prevention and management of adverse events associated with these drugs. EVIDENCE SYNTHESIS: The major findings of the trials and the adverse events are discussed. Prevention and management of common adverse events are addressed. CONCLUSIONS: Zoledronic acid prevents loss of bone mineral density associated with ADT and delays skeletal-related events in metastatic castration-resistant PCa (mCRPC). Denosumab reduces the incidence of fragility fractures associated with ADT, delays the onset of bone metastases in nonmetastatic castration-resistant disease, and is superior to zoledronic acid in the prevention of skeletal complications in mCRPC. Adverse events associated with both agents include osteonecrosis of the jaw and hypocalcemia. Hypocalcemia is more common with denosumab. Zoledronic acid requires dose modifications for renal insufficiency, is contraindicated in severe renal insufficiency, and has been associated with deterioration of renal function. Appropriate patient selection with close attention to dental health, supplementation with calcium and vitamin D, and monitoring of laboratory values are effective strategies to minimize the impact of adverse events associated with osteoclast inhibitors in advanced PCa.

TÍTULO / TITLE: - Outcomes in stage I testicular seminoma: A population-based study of 9193 patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Beard CJ; Travis LB; Chen MH; Arvold ND; Nguyen PL; Martin NE; Kuban DA; Ng AK; Hoffman KE
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Dana-Farber Cancer Institute/Brigham and Women’s Hospital, Boston, Massachusetts.
RESUMEN / SUMMARY: - BACKGROUND: Few studies have quantified temporal patterns of cause-specific mortality in contemporary cohorts of men with early-stage seminoma. Given that several management strategies can be applied in these patients, each resulting in excellent long-term survival, it is important to evaluate associated long-term sequelae. In particular, data describing long-term risks of cardiovascular disease (CVD) are conflicting. METHODS: We identified 9193 men diagnosed with stage I seminoma (ages 15-70 years) in the population-based SEER registries (1973-2001). We calculated survival estimates, standardized mortality ratios (SMRs), and adjusted hazard rates (AHRs). RESULTS: During 121,037 person-years of follow-up (median, 12.3 years), 915 deaths (SMR, 1.23; 95% CI, 1.16-1.32) were reported, with
significant excesses for suicide (n = 39; SMR, 1.45; 95% CI, 1.06-1.98),
infection (n = 58; SMR, 2.32; 95% CI, 1.80-3.00), and second malignant
neoplasms (SMNs; n = 291; SMR, 1.81; 95% CI, 1.61-2.03), but not CVD (n =
201; SMR, 0.91; 95% CI, 0.80-1.05). After radiotherapy (78% patients), CVD
deaths were not increased (n = 158; SMR, 0.89; 95% CI, 0.76-1.04), in contrast
to SMN deaths (n = 246; SMR, 1.89; 95% CI, 1.67-2.14). SMN mortality was
higher among patients administered radiotherapy than among those not given
radiotherapy (AHR, 1.36; 95% CI, 0.99-1.88; P = .059), with a cumulative 15-
year risk of 2.64% (95% CI, 2.19-3.16). Suicide, although rare, accounted for 1
in 230 deaths. CONCLUSIONS: Modern radiotherapy as applied in this large
population-based study is not associated with excess CVD mortality. Although
increased all-cause mortality exists, cumulative SMN risk is considerably
smaller than reported in historical series, but additional follow-up will be
required to characterize long-term trends. The increased risk of suicide,
previously unreported in men with stage I seminoma, requires confirmation.
Cancer 2013. © 2013 American Cancer Society.

[75]
TITULO / TITLE: - Quality of life after prostate cancer treatments in patients
comparable at baseline.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Br J Cancer. 2013 Mar 14;108(9):1784-9. doi:
AUTORES / AUTHORS: - van Tol-Geerdink JJ; Leer JW; van Oort IM; van Lin EJ;
Weijerman PC; Vergunst H; Witjes JA; Stalmeier PF
INSTITUCION / INSTITUTION: - Department of Radiation Oncology, Radboud
University Medical Centre, PO Box 9101, Nijmegen, The Netherlands.
RESUMEN / SUMMARY: - Background: Previous studies on the effects of different
prostate cancer treatments on quality of life, were confounded because patients
were not comparable. This study examined treatment effects in more
comparable groups. Methods: From 2008-2011, 240 patients with localised
prostate cancer were selected to be eligible for both radical prostatectomy (RP)
and external beam radiotherapy (EBRT). Brachytherapy (BT) was a third option
for some. Health-related quality of life was measured by expanded prostate
cancer index composite (EPIC) up to 12 months after treatment. Results: In the
sexual domain, RP led to worse summary scores (P<0.001) and more often to a
clinically relevant deterioration from baseline than BT and EBRT (79%, 33%, 34%,
respectively). In the urinary domain, RP also led to worse summary scores (P=0.014),
and more deterioration from baseline (41%, 12%, 19%, respectively). Only on the irritative/obstructive urinary scale, more BT patients
(40%) showed a relevant deterioration than RP (17%) and EBRT patients
In the bowel domain, the treatment effects did not differ. Conclusion: This study provides a more unbiased comparison of treatment effects, as men were more comparable at baseline. Our results suggest that, for quality of life, radiotherapy is as least as good an option as RP for treating localised prostate cancer.

[76]

TÍTULO / TITLE: Plerixafor and autologous stem cell transplantation: impressive result in a chemoresistant testicular cancer patient treated with high-dose chemotherapy.

RESUMEN / SUMMARY: Plerixafor, a CXCR4 antagonist, induces the rapid release of hematopoietic progenitor stem cells from the bone marrow into peripheral blood; it is approved for autologous hematopoietic progenitor stem cell mobilization in multiple myeloma and non-Hodgkin’s lymphoma patients. We report the case of a 34-year-old patient with metastatic testicular embryonal carcinoma who was extensively and in vain pretreated with chemotherapy and failed to mobilize an adequate number of hematopoietic progenitor stem cells following high-dose chemotherapy, with the support of granulocyte colony-stimulating factors. After a cycle of high-dose cyclophosphamide associated with granulocyte colony-stimulating factors, plerixafor was administered to the patient, with the clinical evidence of an increase in hematopoietic progenitor stem cells in the peripheral blood. The patient achieved a complete engraftment following two cycles of high-dose chemotherapy (paclitaxel, ifosfamide, carboplatin, etoposide), with the support of hematopoietic progenitor stem cells; the patient showed discrete tolerability to the treatment. At biochemical control, the beta-human chorionic gonadotropin value decreased from 86 to less than 1.2 mUI/ml and total body PET-CT scan showed a complete response to chemotherapy. According to this experience, we believe that in patients with advanced germ cell cancer, it is essential to explore the possibility of the use of high-dose chemotherapy to induce a stable and permanent response; in this...
context, plerixafor, with the support of granulocyte colony-stimulating factors, may be an innovative option for satisfactory mobilization during high-dose chemotherapy protocols.
escalation, the use of FMIGRT in radical radiotherapy for prostate cancer significantly reduces the incidence of gastrointestinal toxicity and the duration of late genitourinary toxicity when compared to conventional non-FMIGRT techniques.

[78]

**TÍTULO / TITLE:** - The Impact of Histology on Clinicopathologic Outcomes for Patients With Renal Cell Carcinoma and Venous Tumor Thrombus: A Matched Cohort Analysis.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Kaushik D; Linder BJ; Thompson RH; Eisenberg MS; Lohse CM; Cheville JC; Leibovich BC; Boorjian SA

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Mayo Clinic, Rochester, MN.

**RESUMEN / SUMMARY:** - OBJECTIVE: To evaluate the impact of tumor histology on clinicopathologic outcomes for patients with renal cell carcinoma (RCC) and venous tumor thrombus (VTT). METHODS: We identified 807 patients with RCC and VTT who underwent nephrectomy at our institution between 1970 and 2008. All pathologic specimens were re-reviewed by a single urologic pathologist. Patients with non-clear cell RCC (non-ccRCC, n = 56) were matched 1:2 to patients with clear cell RCC (ccRCC) VTT based on symptoms at presentation, regional lymph node involvement, distant metastases, tumor thrombus level, nuclear grade, and sarcomatoid differentiation. Survival was estimated using the Kaplan-Meier method and compared with the log-rank test. RESULTS: The 56 patients with non-ccRCC VTT included 26 papillary, 11 chromophobe, 5 collecting duct tumors, and 14 RCCs not otherwise specified. Compared to unmatched patients with ccRCC VTT (n = 751), patients with non-ccRCC VTT presented with larger tumor size (P = .02), higher nuclear grade (P = .04), and more frequent sarcomatoid differentiation (P <.001) and lymph node invasion (P <.001). However, when patients with non-ccRCC were matched to patients with ccRCC, no significant differences were noted with regard to 5-year metastases-free survival (41% vs 34%, P = .24) or cancer-specific survival (25% vs 27%, P = .97). CONCLUSION: Non-ccRCC VTT is associated with a high rate of adverse pathologic features. Nevertheless, when matched to patients with ccRCC, patients with non-ccRCC VTT did not have increased rate of recurrence or adverse survival. Aggressive surgical resection represents the mainstay of treatment in these cases, whereas continued efforts to optimize a multimodal management approach to such patients remain necessary.
Mortalidad después de la prostatectomía radical o radioterapia externa para cáncer de próstata localizado.

**RESUMEN / SUMMARY:**
Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:**

**AUTORES / AUTHORS:**
Hoffman RM; Koyama T; Fan KH; Albertsen PC; Barry MJ; Goodman M; Hamilton AS; Potosky AL; Stanford JL; Stroup AM; Penson DF

**INSTITUCIÓN / INSTITUTION:**
Vanderbilt University Medical Center, 2525 W End Ave, Ste 600, Nashville, TN 37203-1738. david.penson@vanderbilt.edu

**RESUMEN / SUMMARY:**
Background No randomized trials have compared survival outcomes for men with localized prostate cancer (PC) being treated with radical prostatectomy (RP) or external beam radiotherapy (EBRT). The goal of the study, therefore, was to estimate the association of RP (compared with EBRT) with overall and PC mortality. Methods We analyzed an observational cohort from the population-based Prostate Cancer Outcomes Study, which included men aged 55 to 74 years diagnosed with localized PC between October 1994 and October 1995 who underwent either RP (n = 1164) or EBRT (n = 491) within 1 year of diagnosis. Patients were followed until death or study end (December 31, 2010). Overall and disease-specific mortality were assessed with multivariable survival analysis, with propensity scores to adjust for potential treatment selection confounders (demographics, comorbidities, and tumor characteristics). All statistical tests were two-sided. Results After 15 years of follow-up, there were 568 deaths, including 104 from PC. RP was associated with statistically significant advantages for overall (hazard ratio [HR] = 0.60, 95% confidence interval [CI] = 0.53 to 0.70, P <.0001.) and disease-specific mortality (HR = 0.35, 95% CI = 0.26 to 0.49, P <.0001.). Mortality benefits for RP were also observed within treatment propensity quintiles, when subjects were pair-matched on propensity scores, and in subgroup analyses based on age, tumor characteristics, and comorbidity. Conclusions Population-based observational data on men diagnosed with localized PC in the mid-1990s suggest a mortality benefit associated with RP vs EBRT. Possible explanations include residual selection bias or a true survival advantage. Results might be less applicable for men facing treatment decisions today.

[79]

[80]
TÍTULO / TITLE: - Quantified KLK15 Gene Expression Levels Discriminate Prostate Cancer From Benign Tumors and Constitute a Novel Independent Predictor of Disease Progression.

RESUMEN / SUMMARY: - BACKGROUND: Several transcript variants of the kallikrein-related peptidase 15 gene (KLK15) have been identified up to now. The classical KLK15 mRNA isoform encodes for a non-truncated, functional protein. Aberrant KLK15 expression is found in breast, ovarian, and prostate cancers. Our aim in this present study was the specific quantitative expression analysis of the classical KLK15 mRNA transcript in prostate tumors and the examination of its clinical significance in prostate cancer. METHODS: We isolated total RNA from 150 prostate tissue specimens and, following cDNA synthesis, the expression of KLK15 classical mRNA transcript was measured via quantitative Real-Time PCR using the TaqMan® chemistry. HPRT1 was used as a reference gene, and the absolute quantification approach, through the incorporation of standard curves, was applied for the calculation of normalized KLK15 expression. RESULTS: KLK15 expression levels were significantly upregulated in malignant compared to benign samples (P < 0.001). The discriminatory value of KLK15 was confirmed by ROC curve and logistic regression analysis (both P < 0.001). KLK15 was also associated with advanced pathological stage (P = 0.023). KLK15-positive prostate cancer patients presented significantly shorter progression-free survival intervals, determined by biochemical relapse (P = 0.006), compared to KLK15-negative ones. Multivariate Cox regression analysis revealed that KLK15 expression is an independent predictor of biochemical recurrence (HR = 3.36, P = 0.038). CONCLUSIONS: The present study unravels the important role of quantified KLK15 classical mRNA expression levels as a novel biomarker helpful for the differential diagnosis and prognosis of prostate cancer patients. Prostate 9999: XX-XX, 2013. © 2013 Wiley Periodicals, Inc.

[81]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

TÍTULO / TITLE: - Epithelial Cell Adhesion Molecule-positive Circulating Tumor Cells as Predictive Biomarker in Patients With Prostate Cancer.

RESUMEN / SUMMARY: - OBJECTIVE: To assess the use of circulating tumor cells (CTCs) as a longitudinal endpoint factor for clinical monitoring of patients with prostate cancer and to evaluate the association among the baseline CTC number, various clinical characteristics, and survival. MATERIALS AND METHODS: The CTCs were enumerated using the CellSearch Food and Drug Administration-cleared CTC kit in 202 patients with prostate cancer. Variables, including metastatic site, prostate-specific antigen level, Gleason score, testosterone level, and use of androgen treatment, were tested for association with the CTC number. The probability of patient survival over time was estimated using the Kaplan-Meier method. RESULTS: The baseline CTC numbers were strongly associated with survival (P <.0001), with overall survival significantly poorer in patients with >/=5 CTCs. Significantly greater CTC numbers were observed in patients with bone metastasis (mean 41.12 CTCs) than in those with lymph node metastasis (mean 2.53 CTC, P = .026). Analysis of the association between the CTC count and prostate-specific antigen level revealed a weak positive correlation (correlation coefficient r = 0.2695, P = .0007). The CTC number also correlated with the Gleason score (P = .0138) and lower testosterone level (P <.0001). Patients without androgen depletion had significantly lower CTC numbers (mean 2.70) than those with androgen depletion (mean 26.39, P <.0001). CONCLUSION: The baseline CTC counts were predictive of patient survival and correlated significantly with the clinical characteristics of patients with prostate cancer. Our study results have confirmed previous findings that support the use of CTC enumeration as a prognostic biomarker for patients with prostate cancer.
[83] **TÍTULO / TITLE:** Re: association of polymorphisms in oxidative stress genes with clinical outcomes for bladder cancer treated with bacillus calmette-guerin.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** Wood DP

[84] **TÍTULO / TITLE:** Statin Use in Relation to Prostate Cancer Outcomes in a Population-based Patient Cohort Study.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
**REVISTA / JOURNAL:** Prostate. 2013 Apr 30. doi: 10.1002/pros.22671.
**AUTORES / AUTHORS:** Geybels MS; Wright JL; Holt SK; Kolb S; Feng Z; Stanford JL
**INSTITUCIÓN / INSTITUTION:** Department of Epidemiology, GROW School for Oncology and Developmental Biology, Maastricht University, Maastricht, The Netherlands.
**RESUMEN / SUMMARY:** BACKGROUND: We investigated associations between statin use begun before prostate cancer (PCa) diagnosis and PCa recurrence/progression and PCa-specific mortality (PCSM) in a prospective, population-based cohort study. METHODS: The analysis included 1,001 PCa patients diagnosed in 2002-2005 in King County, Washington. Statin use was assessed at the time of diagnosis using a detailed in-person interview. Prostate cancer recurrence/progression events and cause-specific survival were ascertained from a follow-up survey and the SEER registry. Multivariable competing risk and Cox proportional hazards regression models were used to assess the risk of PCa outcomes according to categories of statin use.
RESULTS: Of the 1,001 PCa patients in our study, 289 men were ever users of statin drugs. During follow-up, we identified 151 PCa recurrence/progression events and 123 total deaths, including 39 PCa-specific deaths. In unadjusted analysis, the risk of PCSM was significantly lower for statin users compared to non-users (1% vs. 5% at 10 years; P < 0.01). In multivariable analysis, the adjusted hazard ratio of PCSM for statin users versus non-users was 0.19 (95% CI: 0.06, 0.56). Statin use was not associated with overall PCa recurrence/progression and other-cause mortality. CONCLUSIONS: Statin use begun before PCa diagnosis was unrelated to PCa recurrence/progression but was associated with a decrease in risk of PCSM. Prostate 9999:XX-XX. © 2013 Wiley Periodicals, Inc.
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[TÍTULO / TITLE]: - Clinical Significance of Expression of Cancer/testis Antigen and Down-regulation of HLA Class-I in Patients with Stage I Non-small Cell Lung Cancer.

[RESUMEN / SUMMARY]: - Enlace al Resumen / Link to its Summary


[AUTORES / AUTHORS]: - Hanagiri T; Shigematsu Y; Shinohara S; Takenaka M; Oka S; Chikaishi Y; Nagata Y; Baba T; Uramoto H; So T; Yamada S

[INSTITUCIÓN / INSTITUTION]: - Second Department of Surgery, School of Medicine, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan. hanagiri@med.uoeh-u.ac.jp.

[RESUMEN / SUMMARY]: - Aim: The purpose of this study was to investigate the clinical significance of expression of cancer/testis (CT) antigen and down-regulation of HLA class-I in patients with stage I non-small cell lung cancer (NSCLC), which underwent complete surgical resection. PATIENTS AND METHODS: The expression of HLA class-I molecules was evaluated in 136 resected NSCLC specimens by immunohistochemistry. The results were scored as the percentage of stained tumor cells and categorized into two groups: 0-79%, reduced expression; and >80%, normal expression. The expression of CT antigen was performed by reverse transcription-polymerase chain reaction (RT-PCR). RESULTS: The expression of HLA class-I was normal in 49 tumors (36%), and there was reduced expression in 87 tumors (64%). The expression of Melanoma antigen (MAGE)-A3, MAGE-A4, and Kitakyushu lung cancer antigen-1 (KK-LC-1) was positive in 34 (25.0%), 22 (16.2%), and 42 (30.9%) patients, respectively. There was no significant difference in the proportion of HLA class-I expression associated with the expression of any of the CT antigens. Among the patients with positive expression of at least one of the CT antigens, the 5-year survival rate of the patients with the normal expression of HLA class-I was 87.5%; however, it was 63.4% in patients with the reduced expression of HLA class-I (p=0.0477). CONCLUSION: Reduced expression of HLA class-I was an unfavorable prognostic factor in patients with positive expression of CT antigen, and represents an important hurdle to antigen-based cancer immunotherapy.

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[TÍTULO / TITLE]: - miR-205 negatively regulates the androgen receptor and is associated with adverse outcome of prostate cancer patients.

[RESUMEN / SUMMARY]: - Enlace al Resumen / Link to its Summary


[Enlace al texto completo (gratuito o de pago)] 1038/bjc.2013.131

68
Background: The microRNA-205 (miR-205) has been shown to be deregulated in prostate cancer (PCa). Here we continue to investigate the prognostic and therapeutic potential of this microRNA.

Methods: The expression of miR-205 is measured by qRT-PCR and in situ hybridisation in a well-documented PCa cohort. An AGO2-based RIP-Chip assay is used to identify targets that are verified with western blots, luciferase reporter assay, ELISA and immunohistochemistry.

Results: The expression of miR-205 is inversely correlated to the occurrence of metastases and shortened overall survival, and is lower in castration-resistant PCa patients. The miR-205 expression is mainly localised to the basal cells of benign prostate tissues. Genes regulated by miR-205 are enriched in, for example, the MAPK/ERK, Toll-like receptor and IL-6 signaling pathways. We demonstrate binding of miR-205 to the 3’UTR of androgen receptor (AR) and decrease of both AR transcript and protein levels. This finding was corroborated in the patient cohort were miR-205 expression inversely correlated to AR immunostaining in malignant prostate cells and to serum levels of prostate-specific antigen, an androgen-regulated protein.

Conclusion: Taken together, these findings imply that miR-205 might have therapeutic potential, especially for the castration resistant and currently untreatable form of PCa.
PURPOSE OF REVIEW: Prostate cancer remains the commonest nondermatological cause of cancer in Western men and the second leading cause of cancer death in these men. While low and intermediate-risk prostate cancers make up the vast bulk of prostate cancer diagnoses, it is high-risk prostate cancer that is a much larger killer. Management paradigms for such disease are changing and thus we review the current state of play with the management of these cancers and what the future might hold.

RECENT FINDINGS: High-risk prostate cancer is a heterogeneous beast, with huge variations in disease severity. Hence, management of these cases must be tailored based on specific risk factors of individual patients, and the role for surgery especially in the lower end of the spectrum is increasing.

SUMMARY: The increasing use of radical extirpative surgery might negatively impact functional outcomes but are likely to prolong lives of high-risk prostate cancer sufferers, though more research from well conducted randomized controlled trials is needed to exactly define which patient subpopulations should receive which therapies, in which orders, and at what times.

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BACKGROUND: Chronic kidney disease (CKD) is an independent risk factor for morbidity and mortality in multiple disease processes. However, not much is known about the relationship between breast cancer and CKD. CKD is associated with increased difficulty in breast cancer screening or surveillance due to increased calcifications on mammography. In addition, there is concern regarding the optimization of serum levels of chemotherapeutics in patients with CKD or on hemodialysis. We hypothesized that CKD is an independent risk factor for mortality in patients with breast cancer.

METHODS: A case-matched, retrospective review of a prospectively
maintained database was conducted on patients treated for breast cancer at an academic medical center between 1998 and 2011. Glomerular filtration rates (GFRs) were calculated for each patient at the time of diagnosis, and patients with CKD (GFR < 60 mL/min) were matched in a 1:2 ratio with patients with GFR > 60 mL/min, controlling for age, stage at diagnosis, and race. Primary end points measured were disease-free survival and overall survival. Statistical analysis was performed using Student t-test and Kaplan-Meier. RESULTS: Of the 1223 total patients, 54 (4%) had CKD. One hundred five patients without CKD were matched for age, stage at diagnosis, and race. Mean GFR among patients with and without CKD were 47.6 and 83.2 mL/min, respectively (P < 0.001). The 5-y overall survival was 77% for patients with CKD and 86% for patients without CKD (P = 0.47). Disease-free survival was 64% and 81%, respectively (P = 0.45). CONCLUSION: Based on our data, CKD does not appear to have a significant impact on outcomes in patients with breast cancer.

[90]

TÍTULO / TITLE: - Prevalence of patients with nonmetastatic prostate cancer on androgen deprivation therapy in the United States.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Cetin K; Li S; Blaes AH; Stryker S; Liede A; Arneson TJ
RESUMEN / SUMMARY: - OBJECTIVE: To provide the first comprehensive assessment of the number of men exposed to continuous androgen deprivation therapy (ADT) in the nonmetastatic setting in the United States. METHODS: We assembled 2 point-prevalent cohorts on December 31, 2008: men aged 18-64 years enrolled in commercial health plans (MarketScan) and men aged >/=67 years enrolled in fee-for-service (FFS) Medicare (Medicare 5% sample). We identified men with nonmetastatic prostate cancer who were actively receiving continuous ADT (gonadotropin-releasing hormone agonists or bilateral orchiectomy) for at least 6 months on the point-prevalence date. The number of prevalent ADT users in the national commercially insured (45-64 years) and FFS Medicare (>/=65 years) populations was extrapolated with person-level weights. Using age-specific prevalence estimates derived from the 2 data sources, the number of prevalent users in the entire U.S. male population aged >/=45 years was also estimated. RESULTS: We estimate that 11,935 commercially insured men aged 45-64 years (95% confidence interval [CI], 11,310-12,561) and 115,468 FFS Medicare male beneficiaries aged >/=65
years (95% CI, 112,304-118,633) represented patients with nonmetastatic prostate cancer actively receiving continuous ADT for >/=6 months in the United States on December 31, 2008. Extrapolated to the total U.S. male population aged >/=45 years, this estimate was 188,916 (95% CI, 184,104-193,727).

CONCLUSION: Our findings suggest that a substantial number of men with nonmetastatic prostate cancer are managed with continuous ADT for >/=6 months during the course of their disease.

[91]

**TITULO / TITLE:** - Improving risk stratification in patients with prostate cancer managed by active surveillance: a nomogram predicting the risk of biopsy progression.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - BJU Int. 2013 Apr 2. doi: 10.1111/bju.12112.

**AUTORES / AUTHORS:** - Iremashvili V; Burdick-Will J; Soloway MS

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Miller School of Medicine, University of Miami, Miami, FL, USA.

**RESUMEN / SUMMARY:** - OBJECTIVE: To develop a clinical tool that integrates different risk factors and provides individual predictions of the risk of biopsy progression in patients with prostate cancer managed by active surveillance. MATERIALS AND METHODS: Our analysis included 205 patients on active surveillance, each of whom had had at least two surveillance biopsies. We used the Cox proportional hazard regression model to analyse the association between different risk factors and progression-free survival over successive biopsies. This multivariate model was then used to develop a nomogram. Discrimination and calibration of the nomogram were internally validated using 200 bootstrap resamplings. RESULTS: The median follow-up of patients free of progression was 4.6 years. A total of 58 (28%) patients experienced progression. Factors significantly associated with progression were: overall number of positive cores in the diagnostic and first surveillance biopsies, race and prostate-specific antigen density. The bootstrapping concordance index of the nomogram including these variables was 81%. The nomogram tended to underestimate the probability of progression but it identified fairly accurately the distinct groups of patients at low, intermediate and high risk of progression. CONCLUSIONS: In the development cohort, the nomogram was able to separate patients with respect to their risk of biopsy progression. Since accurate risk stratification is essential to optimize patient care, this tool, if external validation confirms its performance, may prove useful for both the counselling and management of patients with low-volume, Gleason 6 prostate cancer.
**TITULO / TITLE:** - Modeling tumor growth kinetics after treatment with pazopanib or placebo in patients with renal cell carcinoma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Cancer Chemother Pharmacol. 2013 May 29.

- Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2191-0

**AUTORES / AUTHORS:** - Bonate PL; Suttle AB

**INSTITUCIÓN / INSTITUTION:** - Astellas Pharma Global Development, 1 Astellas Way, Northbrook, IL, 60062, USA, peter.bonate@astellas.com.

**RESUMEN / SUMMARY:** - PURPOSE: The purpose of this study is to characterize tumor growth kinetics in patients with renal cell carcinoma (RCC) after treatment with pazopanib or placebo and to identify predictive patient-specific covariates.

**METHODS:** Different tumor growth models that included patient-specific covariates were fit to tumor growth data from Phase 2 (n = 220) and Phase 3 (n = 423) clinical trials using nonlinear mixed-effects modeling. Logistic regression was used to determine whether individual model parameters or covariates were related to occurrence of new lesions. **RESULTS:** A modified Wang model that included a quadratic growth term and a mixture model adequately described the data. Patients in Group 1 (93 %) showed treatment-dependent tumor shrinkage followed by treatment-independent regrowth. Patients in Group 2 (7 %) showed treatment-independent tumor shrinkage that did not regrow. In Group 1, pazopanib 800 mg increased the tumor shrinkage rate by 267 % compared to placebo. Baseline tumor size was dependent on baseline hemoglobin, baseline lactate dehydrogenase, study, and prior nephrectomy. Logistic regression analysis showed that prior radiotherapy, baseline tumor size, tumor shrinkage rate, tumor regrowth rate, study, and treatment (P < 0.01 for all) were all important predictors of new lesions. Patients treated with placebo were approximately twice as likely to develop new lesions than patients treated with pazopanib. **CONCLUSIONS:** Mathematical modeling of tumor growth kinetics can quantify the effect of anticancer therapies. Pazopanib 800 mg was shown to be an effective treatment for RCC that increased the tumor shrinkage rate by 267 % compared with placebo and reduced the likelihood of developing new lesions.

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**TITULO / TITLE:** - WT1 microdeletion and slowly progressing focal glomerulosclerosis in a patient with male pseudohermaphroditism, childhood leukemia, Wilms tumor and cerebellar angioblastoma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Buglyo G; Mehes G; Vargha G; Biro S; Matyus J
INSTITUCIÓN / INSTITUTION: - Department of Human Genetics, Department of Pathology and st Department of Internal Medicine, University of Debrecen, Debrecen, Hungary.

RESUMEN / SUMMARY: - The Wilms tumor 1 (WT1) gene is currently in focus by pediatric nephrologists as its mutations are associated with nephrotic syndrome, especially as part of complex clinical entities like Denys-Drash or Frasier syndrome. Renal failure may also develop in young WAGR patients, whose condition is attributed to a deletion at chromosomal region 11p13. However, only limited data exist on WT1 microdeletions. A 30-year-old male patient, with a history of genital malformations, a Wilms tumor manifested during the treatment of acute lymphoid leukemia (ALL) at the age of 4, and a cerebellar angioblastoma, was referred with proteinuria and a reduced glomerular filtration rate (GFR). Kidney biopsy revealed FSGS. Although all WT1 exons were amplified with polymerase chain reaction (PCR) and sequenced, none of them showed a mutation. However, an formalin-fixed, paraffin-embedded (FFPE) tissue sample of the patient’s childhood Wilms tumor showed WT1-positivity restricted to the renal tumor cells, so the WT1 gene was investigated further. Using quantitative reverse transcription PCR (qRT-PCR), the gene was found to be present in only one copy in the patient’s genomic DNA sample, while both copies were detected in both parents. In the patient’s sister, the proximal region of WT1 was shown to have an extra copy. Evidence suggests that a heterozygous microdeletion of the gene WT1 is responsible for the patient’s disease. It seems reasonable to assume a possible abnormality affecting meiotic crossing over at the WT1 locus in one of the parents.

[94]
TÍTULO / TITLE: - The prognostic significance of vasohibin-1 expression in patients with prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Kosaka T; Miyazaki Y; Miyajima A; Mikami S; Hayashi Y; Tanaka N; Nagata H; Kikuchi E; Nakagawa K; Okada Y; Sato Y; Oya M

INSTITUCIÓN / INSTITUTION: - Department of Urology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan.

RESUMEN / SUMMARY: - Background: We recently isolated vasohibin-1 (VASH1), a novel angiogenic molecule that is specifically expressed in activated vascular endothelial cells (ECs), and the status of VASH1 expression has been documented in various cancer angiogenesis. The aim of this study was to assess the prognostic value of VASH1 expression in prostate cancer
Methods: In this study, we retrospectively analysed the clinical records and evaluated the VASH1 expression of tumour microvessels in 167 patients with PCa who underwent radical prostatectomy. We immunohistochemically examined the microvessels positive for anti-CD34 as microvessel density (MVD) and the microvessels with activated ECs positive for VASH1 density. Results: We found that the VASH1 expression was restricted to ECs in the tumour stroma. VASH1 density was significantly associated with pathological T stage, Gleason score and MVD. The 5-year PSA recurrence-free survival rate was 58.8% in patients with higher VASH1 density (\( \geq 12 \) per mm\(^2\)) and 89.1% in patients with lower VASH1 density (<12 per mm\(^2\)), respectively (\( P < 0.001 \)). Microvessel density was not an independent predictor of PSA recurrence. Multivariate analysis revealed that high VASH1 density was an independent prognostic indicator of PSA recurrence (\( P = 0.007 \), HR=2.950). Conclusion: VASH1 density represents a clinically relevant predictor of patient prognosis and can be a new biomarker that would provide additional prognostic information in PCa.

[95]

TITULO / TITLE: - Safety of en bloc ligation of the renal hilum during laparoscopic radical nephrectomy for renal cell carcinoma: a randomized controlled trial.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Chung JH; Lee SW; Lee KS; Cho WY; Kim TH
INSTITUCIÓN / INSTITUTION: - 1 Department of Urology, Hanyang University College of Medicine, Seoul, Korea.
RESUMEN / SUMMARY: - Abstract Aim: To evaluate the safety of en bloc stapler ligation of the renal vascular pedicle during laparoscopic radical nephrectomy for renal cell carcinoma. Subjects and Methods: Clinical data were collected prospectively from 70 patients who underwent either en bloc stapling of the renal hilum (\( n = 35 \)) (Group A) or the separate ligation method (\( n = 35 \)) (Group B) to treat renal cell carcinoma. To evaluate the incidence of arteriovenous fistula (AVF), blood pressure and heart rate were measured, and abdominal auscultation was performed at 1 month, 3 months, 6 months, and 12 months post-surgery. Abdominal computed tomography was also performed at 6 and 12 months post-surgery. In addition, preoperative characteristics and postoperative outcomes (such as operation time and estimated blood loss [EBL]) were examined. Results: Both operation time and EBL were lower for Group A: operative time, Group A versus Group B, 60.26+/−10.94 minutes versus 67.51+/−10.49 minutes (\( P = .007 \)); EBL, Group A versus Group B, 33.53+/−13.46 mL versus 49.14+/−32.21 mL (\( P = .011 \)). No statistically significant differences
were noted in either of the postoperative variables (blood pressure and heart rate), and there was no clinical evidence of bruit or AVF at 12 months post-surgery. Conclusions: No AVF was observed after en bloc ligation upon clinical follow-up or on radiological evaluation.

[96] TITULO / TITLE: - Differential Androgen Deprivation Therapies with Anti-Androgens of Casodex or MDV3100 vs Anti-Androgen Receptor of ASC-J9 Lead to Promote vs Suppress Prostate Cancer Metastasis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Lin TH; Lee SO; Niu Y; Xu D; Liang L; Li L; Yeh SD; Fujimoto N; Yeh S; Chang C
INSTITUCIÓN / INSTITUTION: - University of Rochester Medical Center, United States;
RESUMEN / SUMMARY: - Despite the fact that androgen deprivation therapy (ADT) can effectively reduce prostate tumor size, its effect on prostate cancer (PCa) metastasis remains unclear. We examined the existing data of the ADT treated PCa patients to analyze therapy effects on primary tumors size, prostate specific antigen (PSA) values, and metastatic incidence. We found the current ADT might lead to primary tumors reduction with PSA decreases, yet metastases increase in some PCa patients. Using in vitro and in vivo metastasis models with human PCa cell lines, we also evaluated the effects of the currently used anti-androgens, Casodex and MDV3100, and the newly developed anti-AR compounds, ASC-J9 and cryptotanshinone (CTS), on PCa cell growth and invasion. In vitro results showing that 10 μM Casodex or MDV3100 treatments suppressed PCa cell growth and reduce PSA level, yet significantly enhanced PCa cells invasion. In vivo mice studies using orthotopic xenograft mouse model also confirmed these results. Mechanism dissection further indicated these Casodex/MDV3100 treatments enhanced the TGF-beta1-->Smad3-->MMP9 pathway, but ASC-J9 and CTS showed promising anti-invasion effects via down-regulation of MMP9 expression. Our findings points out potential risks of the currently used anti-androgens, and provide a potential for the development of a novel strategy targeting both PCa growth and metastasis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Enlace al texto completo (gratuito o de pago) 1093/annonc/mdt138

AUTORES / AUTHORS: - Noonan KL; North S; Bitting RL; Armstrong AJ; Ellard SL; Chi KN

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, BC Cancer Agency, Vancouver Cancer Centre, Vancouver.

RESUMEN / SUMMARY: - BACKGROUND: Abiraterone acetate and enzalutamide both improve outcomes in patients with metastatic castration-resistant prostate cancer (mCRPC). Optimal sequencing for these agents and whether cross-resistance occurs is unknown. METHODS: Multicentre review of patients with mCRPC treated with abiraterone acetate and prednisone after progressing on enzalutamide. Primary objective was to determine abiraterone acetate response. RESULTS: Thirty patients identified from four North American centres. At abiraterone initiation, median age was 70 years (56-84 years); 70% had ECOG performance status of 0-1; all had prior docetaxel. Median prior enzalutamide treatment duration was 41 weeks (6-95 weeks), with 70% (21 of 30) having a >/=30% prostate-specific antigen (PSA) decline. Median abiraterone acetate treatment duration was 13 weeks (1-52). No objective radiographic responses were observed. Median abiraterone time to progression (PSA, objective or symptomatic) was 15.4 weeks [95% confidence interval (CI) 10.7-20.2]. Median overall survival was 50.1 weeks (95% CI 28.3-72.0). Three patients had a >/=30% PSA decline with abiraterone. Two of these patients had PSA progression as best response with prior enzalutamide. CONCLUSIONS: In this study of patients progressing after enzalutamide, treatment with abiraterone was associated with a modest response rate and brief duration of effect. Primary progression on enzalutamide may not preclude a response to abiraterone.

[98]

TÍTULO / TITLE: - Metformin decreases glucose oxidation and increases the dependency of prostate cancer cells on reductive glutamine metabolism.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Fendt SM; Bell EL; Keibler MA; Davidson SM; Wirth GJ; Fiske B; Mayers JR; Schwab M; Bellinger G; Csibi A; Patnaik A; Blouin MJ; Cantley LC; Guarente LP; Blenis J; Pollak MN; Olumi AF; Vander Heiden M; Stephanopoulos G

INSTITUCIÓN / INSTITUTION: - Department of Chemical Engineering, Massachusetts Institute of Technology.

RESUMEN / SUMMARY: - Metformin inhibits cancer cell proliferation and epidemiology studies suggest an association with increased survival in cancer
patients taking metformin, however, the mechanism by which metformin improves cancer outcomes remains controversial. To explore how metformin might directly affect cancer cells, we analyzed how metformin altered the metabolism of prostate cancer cells and tumors. We found that metformin decreased glucose oxidation and increased dependency on reductive glutamine metabolism in both cancer cell lines and in a mouse model of prostate cancer. Inhibition of glutamine anaplerosis in the presence of metformin further attenuated proliferation while increasing glutamine metabolism rescued the proliferative defect induced by metformin. These data suggest that interfering with glutamine may synergize with metformin to improve outcomes in patients with prostate cancer.

[99] TÍTULO / TITLE: - Initial Clinical Sensitivity and Acquired Resistance to MET Inhibition in MET-Mutated Papillary Renal Cell Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Diamond JR; Salgia R; Varella-Garcia M; Kanteti R; Lorusso PM; Clark JW; Xu LG; Wilner K; Eckhardt SG; Ching KA; Lira ME; Schoenmakers EF; Christensen JG; Camidge DR
INSTITUCIÓN / INSTITUTION: - Division of Medical Oncology, University of Colorado Anschutz Medical Campus, Mailstop 8117, 12801 East 17th Ave, Aurora, CO 80045; jennifer.diamond@ucdenver.edu.

[100] TÍTULO / TITLE: - c-Myc phosphorylation by PKCzeta represses prostate tumorigenesis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Kim JY; Valencia T; Abu-Baker S; Linares J; Lee SJ; Yajima T; Chen J; Eroshkin A; Castilla EA; Brill LM; Medvedovic M; Leitges M; Moscat J; Diaz-Meco MT
INSTITUCIÓN / INSTITUTION: - Sanford-Burnham Medical Research Institute, La Jolla, CA 92037, USA.
RESUMEN / SUMMARY: - Studies showing reduced PKCzeta expression or enzymatic activity in different types of human cancers support the clinical relevance of PKCzeta as a tumor suppressor. However, the in vivo role of
PKCζ and its mechanisms of action in prostate cancer remain unclear. Here we demonstrate that the genetic inactivation of PKCζ in mice results in invasive prostate carcinoma in vivo in the context of phosphatase and tensin homolog deficiency. Bioinformatic analysis of human prostate cancer gene-expression sets revealed increased c-Myc transcriptional activity in PKCζ-inactive cells, which correlated with increased cell growth, invasion, and metastasis. Interestingly, PKCζ knockdown or the overexpression of a kinase-inactive mutant resulted in enhanced cell proliferation and invasion in vitro through increased c-Myc mRNA and protein levels and decreased Ser-373 phosphorylation of c-Myc. Analysis of prostate cancer samples demonstrated increased expression and decreased phosphorylation of c-Myc at Ser-373 in PKCζ knockout tumors. In vivo xenograft studies revealed that c-Myc phosphorylation by PKCζ is a critical event in the control of metastasis. Collectively, these results establish PKCζ as an important tumor suppressor and regulator of c-Myc function in prostate cancer.

[101]

TÍTULO / TITLE: - A Novel Method for Predicting Late Genitourinary Toxicity After Prostate Radiation Therapy and the Need for Age-Based Risk-Adapted Dose Constraints.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ahmed AA; Egleston B; Alcantara P; Li L; Pollack A; Horwitz EM; Buyyounouski MK

INSTITUCIÓN / INSTITUTION: - Temple University School of Medicine, Philadelphia, Pennsylvania.

RESUMEN / SUMMARY: - BACKGROUND: There are no well-established normal tissue sparing dose-volume histogram (DVH) criteria that limit the risk of urinary toxicity from prostate radiation therapy (RT). The aim of this study was to determine which criteria predict late toxicity among various DVH parameters when contouring the entire solid bladder and its contents versus the bladder wall. The area under the histogram curve (AUHC) was also analyzed.

METHODS AND MATERIALS: From 1993 to 2000, 503 men with prostate cancer received 3-dimensional conformal RT (median follow-up time, 71 months). The whole bladder and the bladder wall were contoured in all patients. The primary endpoint was grade >/=2 genitourinary (GU) toxicity occurring >/=3 months after completion of RT. Cox regressions of time to grade >/=2 toxicity were estimated separately for the entire bladder and bladder wall. Concordance probability estimates (CPE) assessed model discriminative ability.
Before training the models, an external random test group of 100 men was set aside for testing. Separate analyses were performed based on the mean age (<= 68 vs >68 years). RESULTS: Age, pretreatment urinary symptoms, mean dose (entire bladder and bladder wall), and AUHC (entire bladder and bladder wall) were significant (P<.05) in multivariable analysis. Overall, bladder wall CPE values were higher than solid bladder values. The AUHC for bladder wall provided the greatest discrimination for late bladder toxicity when compared with alternative DVH points, with CPE values of 0.68 for age <=68 years and 0.81 for age >68 years. CONCLUSION: The AUHC method based on bladder wall volumes was superior for predicting late GU toxicity. Age >68 years was associated with late grade >/=2 GU toxicity, which suggests that risk-adapted dose constraints based on age should be explored.

[102]

**TITULO / TITLE:** - Bisphosphonate treatment and renal function in 201 myeloma patients undergoing stem cell transplantation.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Schmitt S; Hielscher T; Baldus C; Neben K; Egerer G; Hillengass J; Raab M; Hose D; Ho AD; Bergner R; Goldschmidt H; Moehler TM

**INSTITUCIÓN / INSTITUTION:** - Department of Medicine V, University of Heidelberg, INF 410, 69120, Heidelberg, Germany.

**RESUMEN / SUMMARY:** - Administration of bisphosphonates (BPs) is an essential supportive treatment for reducing bone-related complications in cancer. Deterioration of renal function is one possible side effect of BPs as well as a clinical feature in multiple myeloma. It has been suggested that the nephrotoxicity of different BPs may differ. We performed a retrospective evaluation of renal function in 201 myeloma patients undergoing myeloablative chemotherapy and treatment with ibandronate (I), pamidronate (P), or zoledronate (Z) for up to 36 months. There was no significant deterioration in mean creatinine clearance (CreaCl) in the entire cohort. The percentage of patients experiencing a decrease in CreaCl >/= 25 % from baseline was 33.0 % in the I group, 44.4 % in the P group and 21.4 % in the Z group, respectively. CreaCl at baseline (P < 0.0001), relapse/progression (P = 0.0019), proteinuria at baseline (P = 0.039), age (P = 0.0031) were identified as significant independent predictors of decrease in renal function. In both descriptive multivariant analyses, we found no evidence of an advantage of any particular BP with respect to effects on renal function. In line with these data, in a subgroup of 90 patients with a baseline CreaCl <90 ml/min, no significant difference was evident between the cohorts of patients treated with different
BPs. Regular treatment with the BPs I, P and Z in myeloma patients undergoing intensive chemotherapy appear to be equally safe for up to 3 years in terms of nephrotoxicity.

[103]
TÍTULO / TITLE: - Four-year allograft survival in a highly sensitized combined liver-kidney transplant patient despite unsuccessful anti-HLA antibody reduction with rituximab, splenectomy, and bortezomib.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Koch M; Graser C; Lehnhardt A; Pollok JM; Kroger N; Verboom M; Thaiss F; Eiermann T; Nashan B
INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary and Transplant Surgery, University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany.
RESUMEN / SUMMARY: - Although donor-specific lymphocytotoxic antibodies are regarded as a contraindication for kidney transplantation (KTx), the data available for liver or combined liver or kidney transplantation (cLkTx) are scarce. Here, we report a case of a highly sensitized young man receiving his sixth liver and second kidney graft. Multiple anti-HLA antibodies were present at the time of transplantation. As a result of suspected antibody-mediated graft damage, the patient was treated with rituximab, plasmapheresis, intravenous immunoglobulins, splenectomy, and bortezomib to decrease the antibody production. So far, patient and allograft survival has reached 4 years despite failure to achieve a permanent reduction of anti-HLA antibodies, and particularly nondonor directed antibodies.

[104]
TÍTULO / TITLE: - Impact of Smoking intensity on Outcomes of Patients with Non Muscle Invasive Bladder Cancer Treated by BCG Immunotherapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ajili F; Kourda N; Karay S; Darouiche A; Chebil M; Boubaker S
INSTITUCIÓN / INSTITUTION: - Laboratory of Human and Experimental Pathology, Pasteur Institute of Tunis, Tunis, Tunisia.
RESUMEN / SUMMARY: - Abstract Background: Cigarette smoking is a well-known risk factor of bladder carcinogenesis. The clinical impact of smoking on
bladder cancer recurrence and response to BCG immunotherapy remains unclear. We sought to investigate the effect of smoking intensity on bladder cancer response to BCG therapy, and the interactions between smoking and clinicopathological factors on bladder cancer recurrence. Methods: Clinical information was obtained from 81 smokers patients (smokers at diagnosis) with NMIBC treated with transurethral resection of the bladder tumor followed by BCG immunotherapy. The distribution of smoking intensity on patient age (≥60 years or <60 years), gender, tumor grade, tumor stage, carcinoma in situ, multiplicity and tumor size was assessed. The effect of cigarette smoking on cancer recurrence was estimated using Cox proportional hazard models and Kaplan-Meier analysis. Results: The results showed that smoking intensity was significantly associated with response to BCG immunotherapy (p = 0.010). Univariate Cox regression analysis of clinicopathologic characteristics showed that PT1 stage, tumor size more than 3 cm and smoking intensity significantly increased the risk of recurrence (respectively, p = 0.006; p = 0.008 and p = 0.012). These results were confirmed by Kaplan-Meier survival curves. In addition, multivariate analysis using Cox regression selected the model involving stage, tumor size and smoking intensity as the quasi-independent predictor of recurrence. Conclusion: These findings suggest that cigarette smoking is an independent predictor for patients with NMIBC. Although the current evidence supports a positive link between smoking intensity and the risk of recurrence on NMIBC treated by BCG immunotherapy, additional studies, are needed before definitive conclusions can be drawn.

[105] TÍTULO / TITLE: - Germline BAP1 Mutations Predispose to Renal Cell Carcinomas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Popova T; Hebert L; Jacquemin V; Gad S; Caux-Moncoutier V; Dubois-d’Enghien C; Richaudneau B; Renaudin X; Sellers J; Nicolas A; Sastre-Garau X; Desjardins L; Gyapay G; Raynal V; Sinilnikova OM; Andrieu N; Manie E; de Pauw A; Gesta P; Bonadona V; Maugard CM; Penet C; Avril MF; Barillot E; Cabaret O; Delattre O; Richard S; Caron O; Benfodda M; Hu HH; Soufir N; Bressac-de Paillerets B; Stoppa-Lyonnet D; Stern MH
INSTITUCIÓN / INSTITUTION: - Institut Curie, Inserm U830, Paris 75248, France.
RESUMEN / SUMMARY: - The genetic cause of some familial nonsyndromic renal cell carcinomas (RCC) defined by at least two affected first-degree relatives is unknown. By combining whole-exome sequencing and tumor profiling in a family prone to cases of RCC, we identified a germline BAP1 mutation.
c.277>G (p.Thr93Ala) as the probable genetic basis of RCC predisposition. This mutation segregated with all four RCC-affected relatives. Furthermore, BAP1 was found to be inactivated in RCC-affected individuals from this family. No BAP1 mutations were identified in 32 familial cases presenting with only RCC. We then screened for germline BAP1 deleterious mutations in familial aggregations of cancers within the spectrum of the recently described BAP1-associated tumor predisposition syndrome, including uveal melanoma, malignant pleural mesothelioma, and cutaneous melanoma. Among the 11 families that included individuals identified as carrying germline deleterious BAP1 mutations, 6 families presented with 9 RCC-affected individuals, demonstrating a significantly increased risk for RCC. This strongly argues that RCC belongs to the BAP1 syndrome and that BAP1 is a RCC-predisposition gene.

[106]
TÍTULO / TITLE: - Strategy for detection of prostate cancer based on relation between prostate specific antigen at age 40-55 and long term risk of metastasis: case-control study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Vickers AJ; Ulmert D; Sjoberg DD; Bennette CJ; Bjork T; Gerdtsson A; Manjer J; Nilsson PM; Dahlin A; Bjartell A; Scardino PT; Lilja H
INSTITUCIÓN / INSTITUTION: - Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, USA.
RESUMEN / SUMMARY: - OBJECTIVE: To determine the association between concentration of prostate specific antigen (PSA) at age 40-55 and subsequent risk of prostate cancer metastasis and mortality in an unscreened population to evaluate when to start screening for prostate cancer and whether rescreening could be risk stratified. DESIGN: Case-control study with 1:3 matching nested within a highly representative population based cohort study. SETTING: Malmo Preventive Project, Sweden. PARTICIPANTS: 21,277 Swedish men aged 27-52 (74% of the eligible population) who provided blood at baseline in 1974-84, and 4922 men invited to provide a second sample six years later. Rates of PSA testing remained extremely low during median follow-up of 27 years. MAIN OUTCOME MEASURES: Metastasis or death from prostate cancer ascertained by review of case notes. RESULTS: Risk of death from prostate cancer was associated with baseline PSA: 44% (95% confidence interval 34% to 53%) of deaths occurred in men with a PSA concentration in the highest 10th of the distribution of concentrations at age 45-49 (>/= 1.6 microg/L), with a similar proportion for the highest 10th at age 51-55 (>/= 2.4 microg/L: 44%, 32% to 56%). Although a 25-30 year risk of prostate cancer metastasis could not be
ruled out by concentrations below the median at age 45-49 (0.68 microg/L) or 51-55 (0.85 microg/L), the 15 year risk remained low at 0.09% (0.03% to 0.23%) at age 45-49 and 0.28% (0.11% to 0.66%) at age 51-55, suggesting that longer intervals between screening would be appropriate in this group. CONCLUSION: Measurement of PSA concentration in early midlife can identify a small group of men at increased risk of prostate cancer metastasis several decades later. Careful surveillance is warranted in these men. Given existing data on the risk of death by PSA concentration at age 60, these results suggest that three lifetime PSA tests (mid to late 40s, early 50s, and 60) are probably sufficient for at least half of men.

[107]
TÍTULO / TITLE: - Investigation of six testicular germ cell tumor susceptibility genes suggests a parent-of-origin effect in SPRY4.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Karlsson R; Andreassen KE; Kristiansen W; Aschim EL; Bremnes RM; Dahl O; Fossa SD; Klepp O; Langberg CW; Solberg A; Tretli S; Magnusson PK; Adami HO; Haugen TB; Grotmol T; Wiklund F
INSTITUCIÓN / INSTITUTION: - Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden.
RESUMEN / SUMMARY: - Recent genome-wide association studies have identified single-nucleotide polymorphisms (SNPs) associated with testicular germ cell tumor (TGCT) risk in the genes ATF7IP, BAK1, DMRT1, KITLG, SPRY4 and TERT. In the present study, we validate these associations in a Scandinavian population, and explore effect modification by parental sex and differences in associations between the major histological subtypes seminoma and non-seminoma. A total of 118 SNPs in the six genes were genotyped in a population-based Swedish-Norwegian sample comprising 831 TGCT case-parent triads, 474 dyads, 712 singletons and 3919 population controls. Seven hundred and thirty-four additional SNPs were imputed using reference haplotypes from the 1000 genomes project. SNP-TGCT association was investigated using a likelihood-based association test for nuclear families and unrelated subjects implemented in the software package UNPHASED. Forward stepwise regression within each gene was applied to determine independent association signals. Effect modifications by parent-of-origin and effect differences between histological subtypes were explored. We observed strong association between SNPs in all six genes and TGCT (lowest P-value per gene: ATF7IP 6.2 x 10-6; BAK1 2.1 x 10-10; DMRT1 6.7 x 10-25; KITLG 2.1 x 10-48; SPRY4 1.4 x 10-29; TERT 1.8 x 10-18). Stepwise regression indicated three independent signals for BAK1 and TERT, two for SPRY4 and one each
for DMRT1, ATF7IP and KITLG. A significant parent-of-origin effect was observed for rs10463352 in SPRY4 (maternal odds ratio = 1.72, paternal odds ratio = 0.99, interaction $P = 0.0013$). No significant effect differences between seminomas and non-seminomas were found. In summary, we validated previously reported genetic associations with TGCT in a Scandinavian population, and observed suggestive evidence of a parent-of-origin effect in SPRY4.

[108]

**TITULO / TITLE:** Minimal residual disease after allogeneic stem cell transplant: a comparison among multiparametric flow cytometry, Wilms tumor 1 expression and chimerism status (Complete chimerism versus Low Level Mixed Chimerism) in acute leukemia.

**RESUMEN / SUMMARY:** Relapse represents the main cause of treatment failure after allogeneic stem cell transplant (allo-SCT). The detection of minimal residual disease (MRD) by multiparametric flow cytometry (MFC), chimerism, cytogenetics and molecular analysis may be critical to prevent relapse. Therefore, we assessed the overall agreement among chimerism (low level mixed chimerism [LL-MC] vs. complete chimerism [CC]), MFC and Wilms tumor 1 (WT1) mRNA to detect MRD and investigated the impact of MRD obtained from the three methods on patient outcome. Sixty-seven fresh bone marrow (BM) samples from 24 patients (17 acute myeloid leukemia [AML], seven acute lymphoblastic leukemia [ALL]) in complete remission (CR) after allo-SCT were investigated at different time points. A moderate agreement was found among the three techniques investigated. A higher concordance between positive results from MFC (75.0% vs. 32.7%, $p = 0.010$) and WT1 (58.3% vs. 29.1%, $p = 0.090$) was detected among LL-MC rather than CC samples. Relapse-free survival (RFS) and overall survival (OS) were found to be higher in MRD negative patients than in MRD positive patients analyzed with MFC and WT1. Our results discourage the use of low autologous signals as the only marker of MRD, and suggest the usefulness of MFC and WT1 real-time quantitative polymerase chain reaction (RQ-PCR) in stratifying patients with respect to risk of relapse.
TÍTULO / TITLE: - Successful interventional treatment of post-biopsy renal artery pseudoaneurysm in pediatric patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Xue R; Wang M; Li Q; Zhao XD; Tang XM; Shi JS; He L; Wang Q; Wang S; Luo XP
INSTITUCIÓN / INSTITUTION: - Laboratory of Clinical Immunology, Institute of Children Pediatric Research, Department of Nephroimmunology, Department of Radiology, Department of Ultrasonic Medicine, Department of Oncological Surgery, Children's Hospital of Chongqing Medical University, and Department of Radiology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China.
RESUMEN / SUMMARY: - Background: With an incidence ranging from 0.01% to 1.0%, renal artery pseudoaneurysm (RAP) is a rare complication after renal biopsy, percutaneous renal surgery, penetrating trauma, and rarely blunt renal trauma. Methods: Percutaneous renal biopsy (PRB) of native kidneys was performed in 1,500 pediatric patients under real-time ultrasonographic guidance at our institution from July 1999 to January 2011. A retrospective review of these cases revealed that 2 patients developed a post-biopsy RAP. The diagnosis of RAP was established using color duplex ultrasonography (US), contrastenhanced computed tomography (CT) and digital substraction angiography (DSA). Results: Two patients developed RAP after 1,500 PRBs were performed (0.13% incidence). In the presented cases, immediate post-bioptic ultrasound showed no abnormalities. A high index of suspicion for RAP was prompted when complications such as unexplained gross hematuria and anemia occurred and the arterial phase of CT showed a well-circumscribed hyperdense area with a contrast enhancement similar to the adjacent arterial vessels. The diagnosis was confirmed by DSA and then the feeding artery of RAP was successfully occluded. After the procedure, the patients recovered and were discharged shortly. Conclusion: RAP is a rare, but potentially life-threatening complication after PRB and can be treated successfully with superselective arterial embolization.

[110]
TÍTULO / TITLE: - First Experience Using Peptide Receptor Radionuclide Therapy in a Patient With Urothelial Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
A 78-year-old man with urothelial carcinoma metastasis after surgical resection of the right kidney, part of the ureter, and urinary bladder in May 2003 and 3 cycles of chemotherapy with cisplatin-gemcitabine was referred for peptide receptor radionuclide therapy (PRRT). Somatostatin-receptor profile was assessed by Ga-labeled lanreotide PET, and PRRT was performed using 3738 MBq (101 mCi) of Y-DOTA-lanreotide. Because of adequate PRRT response confirmed with MRI and F-FDG PET, surgical resection of the solitary cervical metastasis was feasible. Treatment was well tolerated, and the patient remains in complete remission from his urothelial carcinoma.

[111]

TÍTULO / TITLE: - Quality assurance of the EORTC 22043-30041 trial in post-operative radiotherapy in prostate cancer: Results of the Dummy Run procedure.

(22), OAR delineation (23), planning and dosimetry (3) or treatment verification (1). Nine submissions were rejected requiring resubmission, seven for target volume delineation reasons alone. Intervention to highlight the importance of delineation guidelines was made prior to the entry of the first patient in the trial. After this, a lower percentage of resubmissions was required. CONCLUSIONS: The EORTC 22043-30041 Dummy Run highlights the need for timely and effective QART in clinical trials. The variation in target volume and OAR definition demonstrates that clinical guidelines and radiotherapy protocols are not a substitute for QART procedures. Early intervention in response to the Dummy Run improved protocol understanding.

[112]

TÍTULO / TITLE: - Elevation of Receptor Tyrosine Kinases by Small Molecule AKT Inhibitors in Prostate Cancer Is Mediated by Pim-1.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Cen B; Mahajan S; Wang W; Kraft AS

INSTITUCIÓN / INSTITUTION: - Authors’ Affiliations: Department of Medicine; and The Hollings Cancer Center, Medical University of South Carolina, Charleston, South Carolina.

RESUMEN / SUMMARY: - The PI3K/AKT pathway is hyperactivated in prostate cancer but its effective therapeutic targeting has proven difficult. In particular, the antitumor activity of AKT inhibitors is attenuated by upregulation of receptor tyrosine kinases (RTK) through an uncharacterized feedback mechanism. In this report, we show that RNA interference-mediated silencing or pharmacologic inhibition of Pim-1 activity curtails AKT inhibitor-induced upregulation of RTKs in prostate cancer cells. Although Pim kinases have been implicated in cap-dependent translational control, we find that in the context of AKT inhibition, the expression of RTKs is controlled by Pim-1 in a cap-independent manner by controlling internal ribosome entry. Combination of Pim and AKT inhibitors resulted in synergistic inhibition of prostate tumor growth in vitro and in vivo. Together, our results show that Pim-1 mediates resistance to AKT inhibition and suggest its targeting to improve the efficacy of AKT inhibitors in anticancer therapy. Cancer Res; 73(11); 3402-11. ©2013 ACR.

[113]
**TÍTULO / TITLE:** - Risk of Urinary Incontinence following Post-Brachytherapy Transurethral Resection of the Prostate (TURP) and Correlation with Clinical and Treatment Parameters.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Mock S; Leapman M; Stock RG; Hall SJ; Stone NN

**INSTITUCIÓN / INSTITUTION:** - Mount Sinai School of Medicine, New York, New York, United States. Electronic address: stephen.mock@mountsinai.org.

**RESUMEN / SUMMARY:** - PURPOSE: We assess the risk of urinary incontinence (UI) after TURP in patients previously treated with prostate brachytherapy. MATERIALS AND METHODS: A total of 2,495 patients underwent brachytherapy with or without external beam radiation therapy for the diagnosis of prostate cancer between June 1990 and December 2009. Pre-implant patients TURP were excluded. Of these patients, 79 patients (3.3%) underwent channel TURP due to urinary retention or refractory obstructive urinary symptoms. Correlation analyses were performed using chi square (Pearson). Estimates for time to UI were determined by Kaplan Meier method with comparisons by logistic regression and Cox proportions hazard rates.

RESULTS: Median follow up after implantation was 7.2 yrs. Median time to first post-implantation TURP was 14.8 months. Twenty of the 79 (25.3%) post-implant TURP patients had UI compared with 3.1% for implantation only patients (odds ratio 10.4; 95% CI, 6-18; p<0.001). Of the 15 patients who required more than 1 TURP, 8 (53%) developed UI compared with 19% of patients who had only 1 TURP (odds ratio 4.9; 95% CI, 1.5-16; p=0.006). Exclusion of patients with multiple TURPs still demonstrated significant differences (18.8% vs. 3.1%, odds ratio 7.1; 95% CI, 3.6-13.9; p<0.001). Median time from last TURP to UI was 24 months. On linear regression analysis, hormone use and post-implantation TURP were associated with UI (p<0.05). There was no correlation between timing of TURP after implantation and risk of incontinence. CONCLUSIONS: Urinary incontinence developed in 25.3% who underwent TURP following prostate brachytherapy. UI risk correlates with the number of TURPs. Patients should be counseled thoroughly prior to undergoing post-implantation TURP.

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[114]

**TÍTULO / TITLE:** - The predictive value of endorectal 3-Tesla multiparametric MRI for extraprostatic extension in low-, intermediate and high-risk prostate cancer patients.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Somford DM; Hamoen EH; Futterer JJ; van Basten JP; van de Kaa CA; Vreuls W; van Oort IM; Vergunst H; Kiemeney LA; Barentsz JO; Witjes JA

INSTITUCIÓN / INSTITUTION: Department of Urology, Canisius-Wilhelmina Hospital, Nijmegen, The Netherlands; Department of Urology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. Electronic address: r.somford@cwz.nl.

RESUMEN / SUMMARY: PURPOSE: We aimed to determine the positive and negative predictive values of multiparametric MRI (MP-MRI) for extraprostatic extension (EPE) at radical prostatectomy (RP) for different prostate cancer (PCa) risk groups. MATERIALS AND METHODS: We evaluated a cohort of 183 patients that underwent 3 Tesla (3-T) MP-MRI, including T2-weighted, diffusion-weighted MR Imaging (DWI) and dynamic contrast-enhanced (DCE) sequences, with an endorectal coil (ERC) before RP, pathological stage at RP was used as standard reference for EPE. The cohort was classified into low-, intermediate and high-risk groups according to the d’Amico criteria. We recorded prevalence of EPE at RP and determined sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of MP-MRI for EPE in each group. Uni- and multivariable analyses were performed to identify predictors of EPE at RP. RESULTS: Overall prevalence of EPE at RP was 49.7% ranging from 24.7-77.1% between low- and high-risk categories. Overall staging accuracy of MP-MRI for EPE was 73.8%, with sensitivity, specificity, PPV and NPV of 58.2%, 89.1%, 84.1% and 68.3%, respectively. PPV of MP-MRI for EPE was best in the high-risk cohort with 88.8%. NPV was highest in the low-risk cohort with 87.7%. With an odds ratio (OR) of 10.3 MP-MRI is by far the best pre-operative predictor of EPE at RP. CONCLUSIONS: For adequate patient counselling, knowledge of predictive values of MP-MRI for EPE is of utmost importance. High NPV, important for decisions on nerve-sparing strategies at RP, is only reached in low-risk subjects.


RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: You W; Li Z; Jing C; Qian-Wei X; Yu-Ping Z; Weng-Guang L; Hua-Lei L

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INSTITUCIÓN / INSTITUTION: - 1 Department of Urology, Affiliated Hospital of Nantong University, Nantong, Jiangsu, China.
RESUMEN / SUMMARY: - Epidemiological studies have investigated that functional polymorphisms in the methylenetetrahydrofolate reductase (MTHFR) gene may play an essential role in bladder carcinogenesis, but the association between these single-nucleotide polymorphisms in the MTHFR gene and the susceptibility of bladder cancer (BC) was inconsistent in previous studies. The objective of this current study was to conduct an update analysis investigating the association between three polymorphisms in the MTHFR gene and the risk of BC. We performed a meta-analysis of 13 publications involving an association between BC and MTHFR gene three polymorphisms (C677T, A1298C, and G1793A). We assessed the strength of the association, using odds ratios (ORs) with 95% confidence intervals (CIs). On one hand, we found that the C677T polymorphism was associated with increased BC risk among Asians, however, with decreased BC risk among a mixed population. Interestingly, BC patients who carried the T-allele (TT+TC) had a higher percentage than the individuals who carried the CC genotype (OR=1.38, 95% CI=1.13-1.69, p=0.002). On the other hand, the A1298C polymorphism may increase BC risk among Asians and Africans, but played a decreased association among Europeans. Results from the current update analysis suggested that the C677T and A1298C polymorphisms in the MTHFR gene were associated with BC risk and disease progression.

[116]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Stoehr R; Taubert H; Gaisa NT; Smeets D; Kneitz B; Giedl J; Ruemmele P; Wieland WF; Rau TT; Hartmann A
INSTITUCIÓN / INSTITUTION: - Institute of Pathology, University Hospital Erlangen, 91054, Erlangen, Germany.
RESUMEN / SUMMARY: - Recently mutations in the MED12 gene have been reported in 5.4% of prostate tumours from Caucasian patients analysed by exome sequencing (Barbieri et al., 2012). In >70% of prostate tumours with MED12 mutation, a recurrent p.L1224F mutation in exon 26 was found. In order to validate this MED12 p.L1224F mutation an unselected cohort of prostate tumours from Caucasian patients was analysed by Sanger sequencing. Overall, 223 prostate tumours and 3 lymph node metastases were analysed. The MED12 p.L1224F mutation could not be detected in any of the cases. So far, the recently reported MED12 p.L1224F mutation could not be validated in
our unselected cohort of prostate tumours. Contrary to the findings of Barbieri and co-workers our data indicate either, that the p.L1224F mutation in the MED12 gene might play no role in prostate carcinogenesis, or this alteration might only be relevant in a small subgroup of tumours.

[117]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.02.083
AUTORES / AUTHORS: - Laguna MP

[118]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1111/tan.12113
AUTORES / AUTHORS: - Yamada R; Takahashi A; Torigoe T; Morita R; Tamura Y; Tsukahara T; Kanaseki T; Kubo T; Watarai K; Kondo T; Hirohashi Y; Sato N
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Sapporo Medical University School of Medicine, Sapporo, Japan.
RESUMEN / SUMMARY: - Cancer/testis (CT) antigens encoded by CT genes are immunogenic antigens, and the expression of CT gene is strictly restricted to only the testis among mature organs. Therefore, CT antigens are promising candidates for cancer immunotherapy. In a previous study, we identified a novel CT antigen, DNAJB8. DNAJB8 was found to be preferentially expressed in cancer stem-like cells (CSCs)/cancer-initiating cells (CICs), and it is thus a novel CSC antigen. In this study, we hypothesized that CT genes are preferentially expressed in CSCs/CICs rather than in non-CSCs/CICs and we examined the expression of CT genes in CSCs/CICs. The expression of 74 CT genes was evaluated in side population (SP) cells (=CSC) and main population (MP) cells (=non-CSC) derived from LHK2 lung adenocarcinoma cells, SW480 colon adenocarcinoma cells and MCF7 breast adenocarcinoma cells by RT-PCR and real-time PCR. Eighteen genes (MAGEA2, MAGEA3, MAGEA4, MAGEA6, MAGEA12, MAGEB2, GAGE1, GAGE8, SPANXA1, SPANXB1, SPANXC, XAGE2, SPA17, BORIS, PLU-1, SGY-1, TEX15 and CT45A1) showed higher expression levels in SP cells than in MP cells, whereas 10
genes (BAGE1, BAGE2, BAGE4, BAGE5, XAGE1, LIP1, D40, HCA661, TDRD1 and TPTE) showed similar expression levels in SP cells and MP cells. Thus, considerable numbers of CT genes showed preferential expression in CSCs/CICs. We therefore propose a novel sub-category of CT genes in this report: cancer/testis/stem (CTS) genes.

[119]

TÍTULO / TITLE: - Patient and Graft Survival After Pre-emptive Versus Non-pre-emptive Kidney Transplantation: A Single-Center Experience From Turkey.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Bozkurt B; Kumru AO; Dumlu EG; Tokac M; Kocak H; Suleymanlar G; Dinckan A
INSTITUCIÓN / INSTITUTION: - Ataturk Training and Research Hospital, Clinic of Surgery, Organ Transplantation Center, Ankara, Turkey. Electronic address: birkan.bozkurt@gmail.com.

RESUMEN / SUMMARY: - OBJECTIVE: We sought to report the graft and patients survival of pre-emptive and non-pre-emptive kidney transplantations performed in our center. METHODS: The 859 subjects showed a mean age of 36.1 years and included 64.6%; males, who received grafts from living (n = 665) or deceased (n = 194) donors between January 2008 and June 2011. We reviewed their medical records retrospectively, to separately pre-emptive versus non-pre-emptive recipients for year transplant outcomes. RESULTS: Among the 859 patients, 153 (17.8%) underwent pre-emptive and 706 (82.2%), non-pre-emptive kidney transplantations. The rate of living donors was higher in the pre-emptive group (97.4% vs 73%, respectively). The 1-year graft survivals were 99.3% and 95.8% in pre-emptive and non-pre-emptive transplantation groups, respectively (P > .05). There was no significant difference between groups with respect to patient survival at 1 year (P > .05). CONCLUSION: In conclusion, graft and patient survival rates between pre-emptive and non-pre-emptive kidney transplantation cases were comparable at 1 year. Pre-emptive kidney transplantation, which eliminates hemodialysis costs and complications, should be preferred as the optimal renal replacement therapy for end-stage renal disease patients.

[120]
Upper tract imaging surveillance is not effective in diagnosing upper tract recurrences in patients followed for non-muscle-invasive bladder cancer.

PURPOSE: To evaluate the utility in routine upper tract imaging in patients followed for non-muscle-invasive bladder cancer (NMIBC).

MATERIALS AND METHODS: A retrospective review of patients treated for NMIBC between 2000 and 2006 was conducted. Kaplan-Meier curves were calculated to determine upper tract urothelial carcinoma (UTUC)-free probability for stage Ta and T1. Bladder cancer stage was included as a time-dependent covariate. Descriptive statistics were used to report rates of imaging studies used and the efficacy in diagnosing UTUC. RESULTS: Fifty-one of a total of 935 patients treated and followed for NMIBC were diagnosed with UTUC; median follow-up was 5.5 years. Five-year UTUC-free probability among Ta and T1 patients was 98% and 93%, respectively. Ten-year UTUC-free probability among Ta and T1 patients was 94% and 88%, respectively. Only 15 (29%) patients were diagnosed on routine imaging while the others were diagnosed after developing symptoms. Overall, 3074 routine imaging scans were conducted for an overall efficacy of 0.49%. CONCLUSIONS: Upper tract recurrence is a lifelong risk in patients with bladder cancer, but most will be missed on routine upper tract imaging. The majority of UTUCs can been diagnosed using a combination of thorough history taking, physical exam, urine cytology and sonography, indicating that routine surveillance imaging may not be the most efficient way of detecting upper tract recurrences.
OBJECTIVE: To compare the biochemical outcomes reported after radical prostatectomy (RP) versus high dose permanent prostate brachytherapy (HDPPB) using iodine-125 seeds in the treatment of matched high risk prostate cancer (HiPCa).

METHODS: In this retrospective review, 55 HiPCa patients treated between March 2006 and August 2011, who underwent HDPPB using iodine-125 seeds combined with external beam radiation therapy (EBRT) or androgen deprivation therapy (ADT), were compared with 55 HiPCa patients who underwent RP. Patients were matched for age, prostate-specific antigen (PSA), clinical stage, and Gleason scores. The biochemical outcomes after HDPPB and RP were compared via Kaplan-Meier analysis.

RESULTS: Of the 110 patients analyzed, the mean ages, PSA, and Gleason biopsy scores were similar between the two cohorts. Among patients who underwent HDPPB, 20 patients (36.4%) had received adjuvant EBRT. Of this subsample, most patients (98.2%) had received adjuvant ADT for 3 months. Among patients with RP, 20 patients (36.4%) had received adjuvant EBRT, whereas 28 patients had received adjuvant ADT. The mean implanted seed numbers were 92.8, the mean D90 was 218.7 Gy, and the mean V100 was 96.1% after HDPPB. With regard to oncological outcomes, biochemical disease-free survival rates were similar between the two cohorts (82.6 vs. 81.1%, p = 0.982). Urethrorectal fistula developed in one patient with HDPPB.

CONCLUSION: RP and HDPPB, using iodine-125 seeds with combined treatment modalities, exhibited similar biochemical recurrence-free survival rates among HiPCa patients. Further prospective studies with greater sample sizes and longer follow-up periods are needed to validate these results.
of these basic science studies into clinically valuable biomarkers for diagnosis and prognosis and biomarkers that are predictive for therapy is critical to the development of precision medicine in prostate cancer. We review potential applications aimed at improving screening specificity in prostate cancer and differentiating aggressive versus indolent prostate cancers. Furthermore, we review predictive biomarker candidates involving ETS gene rearrangements, PTEN inactivation, and androgen receptor signaling. These and other putative biomarkers may signify aberrant oncogene pathway activation and provide a rationale for matching patients with molecularly targeted therapies in clinical trials. Lastly, we advocate innovations for clinical trial design to incorporate tumor biopsy and molecular characterization to develop biomarkers and understand mechanisms of resistance.

[123]

**TÍTULO / TITLE:** - The diagnostic role of human epididymis protein 4 and serum amyloid-A in early-stage endometrial cancer patients.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Tumour Biol. 2013 May 3.

**AUTORES / AUTHORS:** - Omer B; Genc S; Takmaz O; Dirican A; Kusku-Kiraz Z; Berkman S; Gurdol F

**INSTITUCIÓN / INSTITUTION:** - Department of Biochemistry, Istanbul Faculty of Medicine, Istanbul University, 34093, Capa, Istanbul, Turkey.

**RESUMEN / SUMMARY:** - The aim of this study was to evaluate the prognostic and predictive efficacy of the human epididymis secretory protein 4 (HE4) and serum amyloid-A (S-AA) together with the other tumor markers (CA 125, CA 15-3, CEA, and CA 19-9) in endometrial cancer patients. The study group consisted of 64 patients with defined stage and grade of endometrial cancer and 60 women with benign uterine diseases. Thirty-four healthy women were defined as the control group. Fasting blood samples were collected prior to surgery and tumor marker levels were determined in blood samples by E170 autoanalyzer. S-AA concentrations were measured by particle-enhanced immunonephelometry. Preoperative serum HE4 and S-AA levels were significantly higher in endometrial cancer patients than in controls, whereas the other measured parameters were not significantly different. Serum levels of HE4 were related to both the stage and grade of tumor. The best cutoff point for HE4 was determined to be 59.7 pmol/L; with 75 % sensitivity and 65.5 % specificity. For S-AA, the cutoff point was 8.8 U/mL, with 68.7 % sensitivity and 58.6 % specificity. The combination of HE4, CA 125, CEA, and S-AA raised the sensitivity to 84 %. Preoperative measurement of serum HE4 and S-AA may be of help in early detection of endometrial cancer. Preoperative screening with
these markers may provide important information about the patient’s outcome and prognosis.

[124]
**TÍTULO / TITLE:** Bone Morphogenetic Protein-6 in Renal Cell Carcinoma Promotes Tumor Proliferation via M2 Polarization of Tumor-Infiltrating Macrophages through Interleukin-10.

**RESUMEN / SUMMARY:** Dysregulated BMPs expression may contribute to the development and progression of renal cell carcinoma (RCC). Herein, we report that bone morphogenetic protein-6 (BMP-6) promotes the proliferation of RCC cells by IL-10-mediated polarization of tumor-associated macrophages (TAM). IL-10 secretion from macrophages stimulated by BMP-6 required nuclear interaction between Smad5 and STAT3. Examination of human RCC specimens revealed a three-marker signature composed of BMP-6, IL-10, and CD68 (macrophages) that was associated with a significantly higher probability of dying from cancer. In particular, patients with elevated serum levels of IL-10 had a significantly higher rate of metastasis within 5 years after surgery. Together our results suggested that BMP-6/macrophage/IL-10 autocrine loop regulates M2 polarization of TAMs in RCC and that the disruption of this loop may offer an RCC therapeutic strategy.

[125]
**TÍTULO / TITLE:** Diagnostic Radiation Exposure During Surveillance in Patients With pT1a Renal Cell Carcinoma.

**RESUMEN / SUMMARY:** Dysregulated BMPs expression may contribute to the development and progression of renal cell carcinoma (RCC). Herein, we report that bone morphogenetic protein-6 (BMP-6) promotes the proliferation of RCC cells by IL-10-mediated polarization of tumor-associated macrophages (TAM). IL-10 secretion from macrophages stimulated by BMP-6 required nuclear interaction between Smad5 and STAT3. Examination of human RCC specimens revealed a three-marker signature composed of BMP-6, IL-10, and CD68 (macrophages) that was associated with a significantly higher probability of dying from cancer. In particular, patients with elevated serum levels of IL-10 had a significantly higher rate of metastasis within 5 years after surgery. Together our results suggested that BMP-6/macrophage/IL-10 autocrine loop regulates M2 polarization of TAMs in RCC and that the disruption of this loop may offer an RCC therapeutic strategy.
RESUMEN / SUMMARY: - OBJECTIVE: To determine the pattern of postoperative radiographic surveillance in patients with pT1a renal cell carcinoma (RCC) at a tertiary care hospital. METHODS: An institutionally approved urologic oncology database was used to retrospectively identify patients who underwent partial or radical nephrectomy for pT1a RCC from 1990 to 2010 at a tertiary care center. Baseline characteristics were reviewed, and postoperative imaging for the indication of RCC surveillance was recorded. Radiation exposure was calculated using the effective dose according to imaging modality. Relative risks of the development of solid malignancies and leukemia were calculated from the dose of radiation exposure. RCC recurrence, defined as radiologic evidence of local recurrence or distant metastases, was noted. RESULTS: A total of 1708 patients had undergone partial or radical nephrectomy for a renal mass. Of these, 315 patients had pT1a RCC with postsurgical follow-up, and 252 (80%) of these patients were exposed to ionizing radiation during postoperative surveillance. Mean radiation doses in years 1, 2 to 5, and >/=6 after surgery were 11.4, 47.0, and 13.8 mSv, respectively. Relative risks of radiation-induced solid cancers and leukemia were 1.05 and 1.12, respectively. There were 8 (2.5%) total recurrences. CONCLUSION: During the past 20 years, 80% of patients undergoing surgery for pT1a RCC were monitored with radiation-based imaging during postoperative surveillance. Given the low rate of cancer recurrence in this population, expanded efforts in counseling physicians regarding the risk of ionizing radiation in imaging should be encouraged.

[126]
TITULO / TITLE: - Sorafenib and Everolimus in Advanced Clear Cell Renal Carcinoma: A Phase I/II Trial of the SCRI Oncology Research Consortium.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
-autor(es) / authors: Hainsworth JD; Waterhouse DM; Penley WC; Shipley DL; Thompson DS; Webb CD; Anthony Greco F
INSTITUCIÓN / INSTITUTION: - Sarah Cannon Research Institute, Nashville, Tennessee, USA, 1.
RESUMEN / SUMMARY: - Purpose: To evaluate the feasibility and efficacy of sorafenib and everolimus in renal cell carcinoma (RCC). Methods: Patients with advanced RCC and </=1 previous targeted therapy were treated. Results: Maximum tolerated doses were sorafenib 200 mg PO BID, everolimus 35 mg PO once weekly. Dose-limiting toxicity was hand-foot syndrome. The response rate was 13%; median PFS was 5.45 months (95% CI: 3.8-7.6). Skin toxicity, fatigue, hypertension, proteinuria, and mucositis (usually Grade 2) were
common. Conclusions: Fifty percent doses of sorafenib and everolimus were required when these drugs were combined. No increase in efficacy was suggested; toxicity was modestly increased.


AUTORES / AUTHORS: - Repetto L; Abbatecola AM; Paolisso G


AUTORES / AUTHORS: - Crouzet S; Chapelon JY; Rouviere O; Mege-Lechevallier F; Colombel M; Tonoli-Catez H; Martin X; Gelet A

INSTITUCIÓN / INSTITUTION: - Hospices Civils de Lyon, Department of Urology and Transplantation Surgery, Edouard Herriot Hospital, Lyon, France; Inserm, U1032, LabTau, Universite de Lyon, Lyon, France. Electronic address: sebastien.crouzet@chu-lyon.fr.

RESUMEN / SUMMARY: - BACKGROUND: High-intensity focused ultrasound (HIFU) is a nonsurgical therapy for selected patients with localized prostate cancer (PCa). OBJECTIVE: The long-term oncologic and morbidity outcomes of primary HIFU therapy for localized PCa were evaluated in a prospective, single-arm, single-institution cohort study. DESIGN, SETTING, AND PARTICIPANTS: Participants were patients treated with HIFU for localized PCa from 1997 to 2009. Excluded were patients with local recurrence following radiotherapy. A second HIFU session was systematically performed in patients with biopsy-proven local recurrence. INTERVENTION: Whole-gland prostate ablation with transrectal HIFU. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Incontinence was assessed using the Ingelman-Sundberg score, and potency was assessed using the five-item version of the International Index of Erectile Function (IIEF-5) scores. Primary outcomes were
survival rates (biochemical-free, cancer-specific, metastasis-free, and overall survival). Secondary outcomes were morbidity rates. Median follow-up was 6.4 yr (range: 0.2-13.9). The Kaplan-Meier method was used to determine survival estimates, and multivariate analysis was used to determine predictive factors of biochemical progression.

RESULTS AND LIMITATIONS: A total of 1002 patients were included. The median nadir prostate-specific antigen (PSA) was 0.14 ng/ml, with 63% of patients reaching a nadir PSA ≤0.3 ng/ml. Sixty percent of patients received one HIFU session, 38% received two sessions, and 2% received three sessions. The 8-yr biochemical-free survival rates (Phoenix definition) were 76%, 63%, and 57% for low-, intermediate-, and high-risk patients, respectively (p < 0.001). At 10 yr, the PCa-specific survival rate and metastasis-free survival rate (MFSR) were 97% and 94%, respectively. Salvage therapies included external-beam radiation therapy (EBRT) (13.8%), EBRT plus androgen-deprivation therapy (ADT) (9.7%), and ADT alone (12.1%). Severe incontinence and bladder outlet obstruction decreased with refinement in the technology, from 6.4% and 34.9% to 3.1% and 5.9%, respectively. Limitations included the fact that the study was a single-arm study without a comparison group, technological improvements, changes in surgical protocol during the study, and the use of ADT to downsize the prostate in 39% of patients. CONCLUSIONS: HIFU is a potentially effective treatment of localized PCa, with a low PCa-specific mortality rate and a high MFSR at 10 yr as well as acceptable morbidity.

[129]

TÍTULO / TITLE: - The Impact of Age and Clinical Factors in Non-muscle-invasive Bladder Cancer Treated with Bacillus Calmette Guerin Therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ajili F; Darouiche A; Chebil M; Boubaker S
INSTITUCIÓN / INSTITUTION: - Laboratory of Human and Experimental Pathology, Pasteur Institute of Tunis, Tunis, Tunisia and.
RESUMEN / SUMMARY: - Abstract Background: Bladder cancer is a disease of older persons, the incidence of which is expected to increase as the population ages. Prognostic factors for local recurrence for patients with non-muscle invasive bladder cancer have not been fully established. The aim of our study was to determine the influence of age on the outcomes of non muscle invasive bladder (NMIBC) cancer treated with intravesical Bacillus Calmette-Guerin (BCG) therapy. Methods: We retrospectively reviewed the clinical and pathologic data of primary NMIBC from 112 patients who were treated with
transurethral resection followed by BCG-immunotherapy. Time follow-up was 30 months. Clinocopathologic characteristics and response to BCG therapy were correlated with age using univariate and multivariate methods of analysis. Results: Univariate analysis showed that age analyzed as a categorical variable was not associated with other clinicopathological characteristics. On the other hand, multivariate analysis showed that only multiplicity, stage and tumor size were independent significant prognosticators. Conclusions: The results of our study have shown that aging has no impact on the outcomes of high-risk NMIBC treated by BCG immunotherapy.

[130]
TÍTULO / TITLE: - Comparative Efficacy of Sunitinib versus Sorafenib as First-Line Treatment for Patients with Metastatic Renal Cell Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Park SJ; Lee JL; Park I; Park K; Ahn Y; Ahn JH; Lee DH; Ahn S; Song C; Hong JH; Kim CS; Ahn H
INSTITUCIÓN / INSTITUTION: - Department of Oncology, Asan Medical Centre, University of Ulsan College of Medicine, Seoul, Korea.
RESUMEN / SUMMARY: - Background: This study investigated the efficacy and toxicity of sorafenib and sunitinib as primary treatment for patients with metastatic renal cell carcinoma (mRCC). Methods: We identified 49 and 220 patients treated with sorafenib and sunitinib, respectively, as first-line therapy in the Asan Medical Centre from April 2005 to March 2011. Results: Disease control rates of 71 and 74% were achieved with sorafenib and sunitinib, respectively (p = 0.687). After a median follow-up of 27.6 months, progression-free survival (PFS) and overall survival (OS) were not significantly different between the sorafenib and the sunitinib group (PFS 8.6 vs. 9.9 months, respectively, p = 0.948, and OS 25.7 vs. 22.6 months, p = 0.774). Patients treated with sorafenib required dose reduction due to toxicities less frequently than those treated with sunitinib (37 vs. 54%, p = 0.034). Haematological toxicity of grade 3 or 4 was more common in the sunitinib group than in the sorafenib group (45 vs. 4%, p < 0.001). Multivariate analysis showed old age, Heng’s risk group, and bone and liver metastases, but not the type of vascular endothelial growth factor tyrosine kinase inhibitor, were independent prognostic factors affecting OS. Conclusion: The results of this study indicate that sorafenib has comparable efficacy to sunitinib in the treatment of mRCC patients and fewer and less severe toxicities, but the number of patients included in the study was small.
Antitumor T cell responses in bladder cancer are directed against a limited set of antigens and are modulated by regulatory T cells and routine treatment approaches.

Regulatory T cells (Treg) play a key role in cancer immune escape. We identified target antigens of spontaneous tumor-specific T cell responses in urothelial carcinoma (UC) and evaluated their modulation by treatment and Treg. We determined Treg target antigens in UC. Fifty-six UC and thirteen control patients were prospectively enrolled. Blood was drawn before and after routine treatment. Changes in Treg frequency were measured by fluorescence cytometry and the T effector cell (Teff) response against a set of nine tumor-associated antigens (TAA) was monitored with an IFN-gamma ELISpot. Antigen specificity of Treg was determined by their increased capacity to inhibit after TAA-specific activation the proliferation of an autologous T cell population.

The highest difference in the overall response rate for the total T cell population was observed for EGFR (UC: 23%, controls 0%). After depleting Treg also NYESO1 (19%, 0%) and MUC20 (27%, 0%) were more frequently recognized in UC patients. In metastasized patients the TAA-directed T cell response was augmented by Treg depletion. Tumor resection seemed to diminish Treg suppression of TAA-specific immunity, while chemotherapy had no effect. We demonstrated the existence of TAA-specific Treg in UC, which share antigen specificities with Teff. The coexistence of TAA-specific Treg and Teff was very rare. Treg frequencies in the peripheral blood were not changed by therapy. In summary, we identified potentially immunologically relevant TAA in UC. TAA-specific T cell responses against these antigens are suppressed by Treg. We identified TAA-specific Treg in UC patients, which do not cooccur with TAA-specific Teff. © 2013 Wiley Periodicals, Inc.
PURPOSE: This study was designed to assess the independent prognostic value of tumor volume (TV) and whether adding TV provides additional prognostic information for predicting biochemical recurrence (BCR) after radical prostatectomy. METHODS: We reviewed the medical records of 1,129 patients who underwent radical prostatectomy between July 2005 and July 2011. TV was categorized as minimal (≤1.0 ml), moderate (1.1-5.0 ml), or extensive (>5.0 ml). Cox regression analysis was performed to identify independent predictors of BCR. The predictive accuracies of Cox's proportional hazard regression models with and without TV were quantified and compared using time-dependent receiver operating characteristic curve analysis. RESULTS: Increasing TV was associated with higher prostate specific antigen, pathological Gleason score, and pathologic tumor stage. TV was an independent predictor of BCR in multivariate analysis (p < 0.001). When patients were stratified by organ-confined and nonorgan-confined tumor groups, TV remained an independent predictor of BCR in organ-confined tumors (p < 0.001). In the nonorgan-confined tumor group, a significant difference was found only between extensive versus minimal TV (p = 0.023). The predictive accuracy of the Cox regression model increased significantly by adding TV in organ-confined tumor group (0.748 vs. 0.704, p < 0.05) but not in nonorgan-confined group (0.742 vs. 0.734, p > 0.05). CONCLUSIONS: TV was an independent prognostic predictor of BCR in organ-confined prostate cancers and provided additional prognostic information with increased predictive accuracy. In contrast, TV did not increase the predictive accuracy in nonorgan-confined tumor. TV should be considered as a prognosticator in organ-confined tumors.

[133]

TITULO / TITLE: - Transcriptional regulation by the Wilms tumor protein, Wt1, suggests a role of the metalloproteinase Adamts16 in murine genitourinary development.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Jacobi CL; Rudigier LJ; Scholz H; Kirschner KM

INSTITUCIÓN / INSTITUTION: - Charite-Universitaetsmedizin Berlin, Germany.
ADAMTS16 (a disintegrin and metalloproteinase with thrombospondin motifs) is a secreted mammalian metalloproteinase with unknown function. We report here that murine Adamts16 is co-expressed with the Wilms tumor protein, Wt1, in the developing glomeruli of embryonic kidneys. Adamts16 mRNA levels were significantly reduced upon transfection of embryonic murine kidney explants with Wt1 antisense vivo-morpholino. Antisense knockdown of Adamts16 inhibited branching morphogenesis in kidney organ cultures. Adamts16 was detected by in situ mRNA hybridization and/or immuno-histochemistry also in embryonic gonads, and in spermatids and granulosa cells of adult testes and ovaries, respectively. Silencing of Wt1 by transfection with antisense vivo-morpholino significantly increased Adamts16 mRNA in cultured embryonic XY gonads (11.5 and 12.5 d.p.c.), and reduced Adamts16 transcripts in XX gonads (12.5 and 13.5 d.p.c.). Three predicted Wt1 consensus motifs could be identified in the promoter and the 5-untranslated region of the murine Adamts16 gene. Binding of Wt1 protein to these elements was verified by electrophoretic mobility shift assay (EMSA) and chromatin immunoprecipitation (ChIP). A firefly luciferase reporter gene under control of the Adamts16 promoter was activated approximately 8-fold by transient co-transfection of human granulosa cells with a Wt1 expression construct. Gradual shortening of the 5-flanking sequence successively reduced and eventually abrogated Adamts16 promoter activation by Wt1. These findings demonstrate that Wt1 differentially regulates the Adamts16 gene in XX and XY embryonic gonads. It is suggested that Adamts16 acts immediately downstream of Wt1 during murine urogenital development. We propose that Adamts16 is involved in branching morphogenesis of the kidneys in mice.

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**TITULO / TITLE:** - Incidental 11C-Choline PET/CT Brain Uptake due to Meningioma in a Patient Studied for Prostate Cancer: Correlation With MRI and Imaging Fusion.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Bertagna F; Bosio G; Pinelli L; Treglia G; Giubbini R

**INSTITUCIÓN / INSTITUTION:** - From the *Department of Nuclear Medicine and daggerNeuroradiology, University of Brescia and Spedali Civili Brescia, Brescia; and double daggerDepartment of Nuclear Medicine, Catholic University of Sacred Heart, Rome, Italy.

**RESUMEN / SUMMARY:** - We report a case of a 75-year-old male patient treated with radiotherapy in 1999 for prostate cancer. Due to a rise in prostate-specific antigen, he underwent C-choline PET/CT. The study was negative for
secondary lesions but revealed an incidental pathologic focal brain uptake. A subsequent magnetic resonance examination confirmed the presence of a brain lesion typical for meningioma.
TÍTULO / TITLE: - A Kinome-Wide siRNA Screen Identifies Multiple Roles for Protein Kinases in Hypoxic Stress Adaptation, Including Roles for IRAK4 and GAK in Protection against Apoptosis in VHL-/− Renal Carcinoma Cells, Despite Activation of the NF-kappaB Pathway.

RESUMEN / SUMMARY: - Hypoxia induces changes to cancer cells that make them more resistant to treatment. We have looked at signaling pathways that facilitate these changes by screening the human kinome for effects on hypoxic responses in SW480 colon cancer cells. Hits identified in the screen were examined for effects on multiple molecular responses to hypoxia, including the endoplasmic reticulum stress and DNA damage responses in colon, melanoma, and renal cancer lines. To validate the hits from the small interfering RNA studies, we developed cell lines expressing stable short hairpin RNAs (shRNAs) in the A498 renal carcinoma cell line. Several lines, including those expressing shRNAs against DYRK1B, GAK, IHPK2, IRAK4, and MATK, showed an inability to form spheroid cultures. In addition, shRNAs targeting IRAK4 and GAK were incapable of 2D growth under anoxia. In the GAK shRNA-expressing line, nuclear factor-kappaB (NF-kappaB) was localized to the nucleus, but in the IRAK4 shRNA line, NF-kappaB levels were increased but the extent of nuclear localization was unchanged. Dominant negative mutants of IRAK4 and GAK also showed strong apoptotic effects in A498 cells under anoxia, supporting a direct link between these kinases and survival of the VHL-/− RCC line, which is typically highly resistant to hypoxic stress as a result of high and constitutive levels of Hif-1alpha.

[137]

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TÍTULO / TITLE: - Relevance of the mammalian target of rapamycin pathway in the prognosis of patients with high-risk non-muscle invasive bladder cancer.

RESUMEN / SUMMARY: - Hypoxia induces changes to cancer cells that make them more resistant to treatment. We have looked at signaling pathways that facilitate these changes by screening the human kinome for effects on hypoxic responses in SW480 colon cancer cells. Hits identified in the screen were examined for effects on multiple molecular responses to hypoxia, including the endoplasmic reticulum stress and DNA damage responses in colon, melanoma, and renal cancer lines. To validate the hits from the small interfering RNA studies, we developed cell lines expressing stable short hairpin RNAs (shRNAs) in the A498 renal carcinoma cell line. Several lines, including those expressing shRNAs against DYRK1B, GAK, IHPK2, IRAK4, and MATK, showed an inability to form spheroid cultures. In addition, shRNAs targeting IRAK4 and GAK were incapable of 2D growth under anoxia. In the GAK shRNA-expressing line, nuclear factor-kappaB (NF-kappaB) was localized to the nucleus, but in the IRAK4 shRNA line, NF-kappaB levels were increased but the extent of nuclear localization was unchanged. Dominant negative mutants of IRAK4 and GAK also showed strong apoptotic effects in A498 cells under anoxia, supporting a direct link between these kinases and survival of the VHL-/− RCC line, which is typically highly resistant to hypoxic stress as a result of high and constitutive levels of Hif-1alpha.

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INSTITUCIÓN / INSTITUTION: - McGill Urologic Oncology Research, Division of Urology, McGill University Health Center and Research Institute, Montreal, Canada H3G 1W4.
RESUMEN / SUMMARY: - High-risk non-muscle invasive bladder cancer (NMIBC) is associated with higher rates of recurrence and progression. Molecular markers within aberrant signaling pathways in cancer need further evaluation of their role as prognostic indicators and potential future targets for prevention of recurrence. Our objective was to investigate the role of the mammalian target of rapamycin (mTOR) signaling pathway on the stage and outcome of patients with high-risk NMIBC. Tissue microarrays were built from archival bladder tumor specimens (n = 142). Various clinicopathologic variables were collected retrospectively from patients treated with transurethral resection. Immunohistochemical staining was performed for phosphatase and tensin homolog, phosphorylated Akt, phosphorylated mTOR, phosphorylated S6 (p-S6), eukaryotic translation initiation factor 4E-binding protein-1, and p27. Multivariate analysis using Cox regression models addressed recurrence-free survival (RFS), progression-free survival, and worsening-free survival. In multivariate analysis, p-S6 was an independent predictor of shorter RFS (hazard ratio, 3.55; 95% CI, 1.31-9.64). Expression of p27 was inversely correlated with RFS (hazard ratio, 0.27; 95% CI, 0.10-0.74). Low levels of phosphatase and tensin homolog expression were associated with worsening-free survival (P < .03). None of the markers showed correlation with progression-free survival. Our results demonstrate that activation of the mTOR pathway, as assessed by p-S6 and expression of p27, might be used to provide prognostic information, particularly as a predictor of recurrence among patients with high-risk NMIBC.

[138]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1093/ejcts/ezt247
AUTORES / AUTHORS: - Ivert T; Holzmann MJ; Sartipy U
INSTITUCIÓN / INSTITUTION: - Department of Cardiothoracic Surgery and Anaesthesiology, Karolinska University Hospital, Stockholm, Sweden.
RESUMEN / SUMMARY: - OBJECTIVES: The aim was a nationwide analysis of need for dialysis and survival in all patients who had coronary artery bypass grafting (CABG) in Sweden during 2002 up to 2008. METHODS: Primary isolated CABG was performed in 28 220 patients without preoperative need for dialysis. Survival was analysed in patients suffering postoperative acute kidney injury requiring dialysis. RESULTS: Postoperative dialysis was needed in 162
patients (0.6%). Old age, female gender, reduced glomerular filtration rate (GFR), diabetes mellitus, peripheral vascular disease, chronic obstructive pulmonary disease, prior myocardial infarction, prior stroke and reduced left ventricular function were associated with need for dialysis. Only 0.3% of the patients with GFR >60 ml/min/1.73 m2 needed postoperative dialysis compared with 9.5% if GFR was <30 ml/min/1.73 m2. Sixteen of 54 patients (27%) with GFR <30 l/min/1.73 m2 and a >/=50% increase in postoperative serum creatinine needed dialysis. There were 42 deaths (26%) within 30 days in patients who needed dialysis and 1% if dialysis was not required. Early mortality was markedly higher in patients who required dialysis than in those without dialysis after multivariable adjustment for age, sex, diabetes mellitus, left ventricular function and GFR (odds ratio 19, 95% confidence interval 13-29). The corresponding risk of late death was 2-fold higher in patients who survived for 90 days and had required dialysis compared with those who did not (hazard ratio 2.4, 95% confidence interval 1.7-3.3). Five-year survival was 43 and 89%, respectively. The risk of death increased with age. Five-year survival after dialysis was 66% in patients younger than 65 years, but 32% in those aged over 70 years. Fifty-one per cent (14 of 27) of patients 80 years of age or older who required dialysis died early compared with 3% (68 of 2426) of those who did not (P < 0.001). Nine survivors who needed dialysis developed end-stage renal disease. CONCLUSIONS: Need for dialysis after non-emergency was an uncommon serious complication associated with high early mortality and an increased risk of late death. Old age and impaired preoperative renal function were strong predictors of need for dialysis after CABG. Postoperative dialysis after CABG was a marker of poor outcome but could, in some patients, be life-saving.

[139]
TITULO / TITLE: - Evaluation of diagnostic testis biopsy and the repetition of testicular sperm extraction surgeries in infertility patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hussein A
INSTITUCIÓN / INSTITUTION: - Urology Department, Minia University, El-Minia, Egypt. Electronic address: alaymanh@hotmail.com.
RESUMEN / SUMMARY: - OBJECTIVE: To evaluate the use of a diagnostic testis biopsy and a repetition of testicular sperm extraction (TESE) surgeries in azoospermic patients and its impact on the outcome of TESE. DESIGN: Retrospective, case-control study. SETTING: University IVF center and
hospital. PATIENT(S): A total of 552 azoospermic patients undergoing TESE for intracytoplasmic injection. INTERVENTION(S): At the time of the TESE, a piece of testicular tissue was prepared for histopathologic evaluation. MAIN OUTCOME MEASURE(S): Sperm retrieval rate. RESULT(S): Testicular sperm retrieval was successful in 100% of patients with obstructive azoospermia, 95.6% of patients with hypospermatogenesis, 47.9% of patients with maturation arrest, and 28.6% of patients with Sertoli cell-only syndrome in cases with no previous testicular surgery; in 100%, 91.4%, 32%, and 13.3%, respectively, in cases with a history of one testicular surgery; and in 100%, 10%, 0, and 0, respectively, in cases with a history of two testicular surgeries. CONCLUSION(S): Testicular sperm retrieval may be successful for some patients in each histopathologic category of azoospermia, with variable degrees of success for different histopathologic categories. The repetition of testicular surgeries decreases the chance of finding sperm in subsequent testicular sperm retrieval procedures.

[140]

TÍTULO / TITLE: - Combination of Zoledronic Acid and Targeted Therapy Is Active But May Induce Osteonecrosis of the Jaw in Patients With Metastatic Renal Cell Carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Smidt-Hansen T; Folkmar TB; Fode K; Agerbaek M; Donskov F

INSTITUCION / INSTITUTION: - Clinical Fellow, Department of Oncology, Aarhus University Hospital, Aarhus, Denmark. Electronic address: torhan@rm.dk.

RESUMEN / SUMMARY: - PURPOSE: To investigate the efficacy and safety of zoledronic acid (ZA) combined with targeted therapy (TT). MATERIALS AND METHODS: A retrospective study was performed in patients with metastatic renal cell carcinoma treated with ZA and TT. RESULTS: Twenty-one patients received ZA and TT to prevent skeletal-related events and no pretherapy oral and maxillofacial (OM) examination (cohort A). Six patients (29%) developed osteonecrosis of the jaw (ONJ), which was observed only in patients receiving sunitinib and ZA. Sixteen patients received TT and ZA for hypercalcemia and no pretherapy OM examination (cohort B). In these patients, no ONJ was observed. Nine patients received ZA and TT and pretherapy OM examination (cohort C). One patient (11%) developed ONJ during sunitinib and ZA treatment. Mean skeletal morbidity rates were 0.8 for cohort A and 1.2 for cohort C. In the combined cohort (A plus C; n = 30), 47% developed skeletal-related events, 7% pathologic fracture, 7% medullary compression, and 37%
progression of bone metastases. Patients who developed ONJ had a significantly improved median survival of 31.6 months compared with 14.5 months in patients without ONJ (P = .039). CONCLUSION: The combination of ZA and TT resulted in high, clinically meaningful activity. ONJ may be exacerbated by concomitant ZA and sunitinib. Regular OM examinations before and during treatment are recommended.

[141]
TÍTULO / TITLE: - OXER1, a G protein-coupled oxoeicosatetraenoid receptor, mediates the survival-promoting effects of arachidonate 5-lipoxygenase in prostate cancer cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Sarveswaran S; Ghosh J
INSTITUCIÓN / INSTITUTION: - Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI 48202, United States.
RESUMEN / SUMMARY: - Inhibition of 5-Lox induces apoptosis in prostate cancer cells by inactivating PKCepsilon which is prevented by 5-oxoETE, and activators of PKCepsilon prevent 5-Lox inhibition-induced apoptosis, suggesting that 5-Lox metabolites exert survival signaling via PKCepsilon. However, mechanisms by which 5-Lox metabolites activate PKCepsilon are not understood yet. We found that prostate cancer cells express high levels of OXER1, a G protein-coupled 5-oxoETE receptor, which delivers signal by generating diacyl-glycerol through phospholipase C-beta. Interestingly, we found that U73122, an inhibitor of PLC-beta, interrupts the apoptosis-preventing effect of 5-oxoETE, and exogenous diacyl-glycerol effectively prevents 5-Lox inhibition-induced apoptosis, suggesting that 5-oxoETE signals via OXER1 to promote prostate cancer cell survival.

[142]
TÍTULO / TITLE: - Endorectal MRI and MR spectroscopic imaging of prostate cancer: Developing selection criteria for MR-guided focal therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Chang ST; Westphalen AC; Jha P; Jung AJ; Carroll PR; Kurhanewicz J; Coakley FV

110
PURPOSE: To investigate criteria that can identify dominant treatable prostate cancer foci with high certainty at endorectal magnetic resonance imaging (MRI) and MR spectroscopic (MRS) imaging, and thus facilitate selection of patients who are radiological candidates for MR-guided focal therapy. MATERIALS AND METHODS: We retrospectively identified 88 patients with biopsy-proven prostate cancer who underwent endorectal MRI and MRS imaging prior to radical prostatectomy with creation of histopathological tumor maps. Two independent readers noted the largest tumor foci at MRI, if visible, and the volume of concordant abnormal tissue at MRS imaging, if present. A logistic random intercept model was used to determine the association between clinical and MR findings and correct identification of treatable (over 0.5 cm³) dominant intraprostatic tumor foci. RESULTS: Readers 1 and 2 identified dominant tumor foci in 50 (57%) and 58 (65%) of 88 patients; 42 (84%) and 48 (83%) of these were dominant treatable lesions at histopathology, respectively. Within the statistical model, the volume of concordant spectroscopic abnormality was the only factor that predicted correct identification of a dominant treatable lesion on T2-weighted images (odds ratio = 1.75; 95% confidence interval = 1.08 to 2.82; P value = 0.02). In particular, all visible lesions on T2-weighted imaging associated with at least 0.54 cm³ of concordant spectroscopic abnormality were correctly identified dominant treatable tumor foci. CONCLUSION: Patients with dominant intraprostatic tumor foci seen on T2-weighted MRI and associated with at least 0.54 cm³ of concordant MRS imaging abnormality may be radiological candidates for MR-guided focal therapy. J. Magn. Reson. Imaging 2013. © 2013 Wiley Periodicals, Inc.
TÍTULO / TITLE: - Management of an Unusual Case of Intravascular Large B-Cell Lymphoma of the Penis, Prostate, and Bones With CNS Relapse.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wakim JJ; Levenson BM; Mathews D; Naina HV
INSTITUCIÓN / INSTITUTION: - University of Texas Southwestern Medical Center, Dallas, TX.

[145]
TÍTULO / TITLE: - Systematic Structure Modifications of Multi-target Prostate Cancer Drug Candidate Galeterone to Produce Novel Androgen Receptor Down-regulating Agents as an Approach to Treatment of Advanced Prostate Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Njar VC; Godbole AM; Gediya LK; Martin MS; Vasaitis TS; Kwegyir-Aftul AK; Ates-Alagoz Z; Ramalingam S; Purushottamachar P
RESUMEN / SUMMARY: - As part of our program to explore the influence of small structural modifications of our drug candidate, 3beta-(hydroxy)-17-(1H-benzimidazol-1-yl)-androsta-5,16-diene (galeterone, 5) on the modulation of the androgen receptor (AR), we have prepared and evaluated a series of novel C-3, C-16 and C-17 analogs. Using structure activity analysis, we established that the benzimidazole moiety at C-17 is essential and optimal and also that hydrophilic and heteroaromatic groups at C-3 enhance both anti-proliferative (AP) and AR degrading (ARD) activities. The most potent anti-proliferative compounds were 3beta-(1H-imidazole-1-carboxylate)-17-(1H-benzimidazol-1-yl)-androsta-5,16-diene (47), 3-((EZ)-hydroximino)-17-(1H-benzimidazol-1-yl)-androsta-4,16-diene (36), 3beta-(pyridine-4-carboxylate)-17-(1H-benzimidazol-1-yl)-androsta-5,16-diene (43), with GI50 values of 0.87, 1.91 and 2.57 microM, respectively. Compared to 5, compound 47 was 4- and 8-fold more potent with respect to AP and ARD activities, respectively. Importantly, we also discovered that our compounds, including 5, 36, 43 and 47 could degrade both full-length and truncated AR in CWR22rv1 human prostate cancer cells. With these activities, their potential for development as new drugs for the treatment of all forms of prostate cancer.

[146]
TÍTULO / TITLE: - Cost Effectiveness of Fluorescence in Situ Hybridization in Patients with Atypical Cytology for the Detection of Urothelial Carcinoma.
INTRODUCTION: Patients with atypical cytology and equivocal or negative cystoscopies pose a challenging problem due to uncertainty about presence of cancer. In the current study we determined the cost-effectiveness of utilizing FISH assays to determine the need for biopsy in patients with atypical cytology and equivocal or negative cystoscopies.

MATERIALS/METHODS: Data from two large prospective studies evaluating the utility of FISH in the setting of atypical cytology to detect urothelial carcinoma was combined. The data was used to calculate sensitivity and specificity for the Urovysion FISH assay in different clinical scenario. Cost data was obtained from our institution and Medicare reimbursement rates. Evaluation with or without bladder biopsy and with or without upper tract evaluation were considered. RESULTS: The study included 263 patients with atypical cytology and either equivocal (62) or negative (201) cystoscopy. In patients with an equivocal cystoscopy (assuming biopsy done in operating room (OR)), biopsy based on FISH results saved $1740/pt ($3267/pt vs. $1527/pt) and avoided 42 biopsies compared to biopsying all patients. If office based biopsies are used then cost savings using FISH results is $95/pt. In patients with negative cystoscopy, biopsying based on FISH resulted in costs savings of $2241/pt avoiding 167 biopsies compared to biopsying everyone. Assuming office-based biopsy, the cost savings are $216/pt. CONCLUSION: The decision to biopsy patients based on FISH assay in patients with atypical cytology and equivocal or negative cystoscopy was associated with a significant decrease in bladder cancer associated costs.
TÍTULO / TITLE: - 11C-Choline PET/CT Scan in Patients With Prostate Cancer Treated With Intermittent ADT: A Sequential PET/CT Study.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUORES / AUTHORS: - Ceci F; Schiavina R; Castellucci P; Brunocilla E; Fuccio C; Colletti PM; Ferretti A; Chondrogiannis S; Rubello D; Romagnoli D; Malizia C; Martorana G; Fanti S

INSTITUCIÓN / INSTITUTION: - From the *Nuclear Medicine Unit, Department of Haematology Oncology and Laboratory Medicine and daggerDepartment of Urology, Azienda Ospedaliero-Universitaria di Bologna, Policlinico Sant’Orsola-Malpighi, University of Bologna, Bologna, Italy; double daggerNuclear Medicine Unit, Fondazione Salvatore Maugeri, Pavia, Italy; section signDepartment of Radiology, University of Southern California, Los Angeles, CA; and paragraph signDepartment of Nuclear Medicine & PET/CT Centre, Santa Maria della Misericordia Hospital, Rovigo, Italy.

RESUMEN / SUMMARY: - AIM: The purpose of this preliminary study was to evaluate the usefulness of C-choline PET/CT in patients with recurrent prostate cancer and hormone-sensitive disease treated with intermittent antiandrogen therapy scheme. PATIENTS AND METHODS: We retrospectively evaluated 10 patients after radical prostatectomy (n = 8) or external beam radiotherapy (n = 2) as primary therapy, studied with sequential C-choline PET/CT. The first PET/CT (PET1) was performed during antiandrogen therapy (ADT) and the second PET/CT (PET2) was performed after therapy interruption. Only patients with negative results at PET1 were included in the study. At the time of PET1, all patients were under ADT from at least 6 months (mean PSA 0.54 ng/mL). At the time of PET2, all patients had completed ADT for a mean period of 7 months. C-Choline PET/CT findings were validated by a follow-up of at least 12 months or histological confirmation in case of local relapse. RESULTS: PET2 has been able to detect the site of recurrences in all cases. At the time of PET2, mean PSA was 3.88 ng/mL; mean PSAdt was 2.46 months; and mean PSAvel was 6.94 ng/mL/year. Four out of 10 patients showed a single lesion, 5 out of 10 patients showed 2 lesions and 1 patient showed multiple lymph-node lesions. CONCLUSION: When performed during ADT interruption, C-choline PET/CT has been able to detect the site of recurrence in patients with increasing PSA values. In this context, C-choline PET/CT may help to assess the burden of disease or to change the therapeutic approach using more aggressive and addressed therapies like guided RT or salvage lymph-node dissection.
The Steroid Receptor Coactivator-3 Is Required for the Development of Castration-resistant Prostate Cancer.

The transcriptional coactivator SRC-3 plays a key role to enhance prostate cancer (CaP) cell proliferation. Although SRC-3 is highly expressed in advanced CaP, its role in castration resistant CaP (CRPC) driven by PTEN mutation is unknown. We documented elevated SRC-3 in human CRPC and in PTEN-negative human CaP. Patients with high SRC-3 and undetectable PTEN exhibited decreased recurrence-free survival. To explore the causal relationship in these observations, we generated mice in which both Pten and SRC-3 were inactivated in prostate epithelial cells (Pten3CKO mice), comparing them to mice in which only Pten was inactivated in these cells (PtenCKO mice). SRC-3 deletion impaired cellular proliferation and reduced tumor size. Notably, while castration of PtenCKO control mice increased the aggressiveness of prostate tumors relative to non-castrated counterparts, deletion of SRC-3 in Pten3CKO mice reversed all these changes. In support of this finding, castrated Pten3CKO mice also exhibited decreased levels of phospho-Akt, S6 kinase (RPS6KB1) and phosphorylated S6 protein (RPS6), all of which mediate cell growth and proliferation. Moreover, these tumors appeared to be more differentiated as evidenced by higher levels of Fkbp5, an AR-responsive gene that inhibits Akt signaling. Lastly, these tumors also displayed lower levels of certain androgen-repressed genes such as cyclin E2 and MMP10. Together, our results show that SRC-3 drives CRPC formation and offer preclinical proof of concept for a transcriptional coactivator as a therapeutic target to abrogate CRPC progression.

A Knowledge-Based Approach to Improving and Homogenizing Intensity Modulated Radiation Therapy Planning Quality Among Treatment Centers: An Example Application to Prostate Cancer Planning.

A knowledge-based approach to improving and homogenizing intensity modulated radiation therapy planning quality among treatment centers: An example application to prostate cancer planning.
PURPOSE: Intensity modulated radiation therapy (IMRT) treatment planning can have wide variation among different treatment centers. We propose a system to leverage the IMRT planning experience of larger institutions to automatically create high-quality plans for outside clinics. We explore feasibility by generating plans for patient datasets from an outside institution by adapting plans from our institution.

METHODS AND MATERIALS: A knowledge database was created from 132 IMRT treatment plans for prostate cancer at our institution. The outside institution, a community hospital, provided the datasets for 55 prostate cancer cases, including their original treatment plans. For each “query” case from the outside institution, a similar “match” case was identified in the knowledge database, and the match case’s plan parameters were then adapted and optimized to the query case by use of a semiautomated approach that required no expert planning knowledge. The plans generated with this knowledge-based approach were compared with the original treatment plans at several dose cutpoints.

RESULTS: Compared with the original plan, the knowledge-based plan had a significantly more homogeneous dose to the planning target volume and a significantly lower maximum dose. The volumes of the rectum, bladder, and femoral heads above all cutpoints were nominally lower for the knowledge-based plan; the reductions were significantly lower for the rectum. In 40% of cases, the knowledge-based plan had overall superior (lower) dose-volume histograms for rectum and bladder; in 54% of cases, the comparison was equivocal; in 6% of cases, the knowledge-based plan was inferior for both bladder and rectum.

CONCLUSIONS: Knowledge-based planning was superior or equivalent to the original plan in 95% of cases. The knowledge-based approach shows promise for homogenizing plan quality by transferring planning expertise from more experienced to less experienced institutions.
AUTORES / AUTHORS: - Puech P; Rouviere O; Renard-Penna R; Villers A; Devos P; Colombel M; Bitker MO; Leroy X; Mege-Lechevallier F; Comperat E; Ouzzane A; Lemaitre L

INSTITUCIÓN / INSTITUTION: - Departments of Radiology, Urology, Pathology, and Biostatistics, CHRU Lille, Universite Lille Nord de France, Lille, France; INSERM U703, CHRU Lille, Universite Lille Nord de France, Loos, France; Hospices Civils de Lyon, Departments of Urinary and Vascular Radiology, Urology, and Pathology, Hopital Edouard Herriot, Lyon, France; Faculte de Medicine, Universite Lyon 1, Lyon, France; Departments of Radiology, Urology, and Pathology, La Pitie-Salpetriere Hospital, Assistance Publique-Hopitaux de Paris, Faculte de Medicine Pierre and Marie Curie, University Paris VI, Paris, France.

RESUMEN / SUMMARY: - Purpose: To compare biopsy performance of two approaches for multiparametric magnetic resonance (MR)-targeted biopsy (TB) with that of extended systematic biopsy (SB) in prostate cancer (PCa) detection. Materials and Methods: This institutional review board-approved multicenter prospective study (May 2009 to January 2011) included 95 patients with informed consent who were suspected of having PCa, with a suspicious abnormality (target) at prebiopsy MR. Patients underwent 12-core SB and four-core TB with transrectal ultrasonographic (US) guidance, with two cores aimed visually (cognitive TB [TB-COG]) and two cores aimed using transrectal US-MR fusion software (fusion-guided TB [TB-FUS]). SB and TB positivity for cancer and sampling quality (mean longest core cancer length, Gleason score) were compared. Clinically significant PCa was any 3 mm or greater core cancer length or any greater than 3 Gleason pattern for SB or any cancer length for TB. Statistical analysis included t test, paired chi2 test, and kappa statistic. Primary end point (core cancer length) was calculated (paired t test). Results: Among 95 patients (median age, 65 years; mean prostate-specific antigen level, 10.05 ng/mL [10.05 mug/L]), positivity rate for PCa was 59% (n = 56) for SB and 69% (n = 66) for TB (P = .033); rate for clinically significant PCa was 52% (n = 49) for SB and 67% (n = 64) for TB (P = .0011). Cancer was diagnosed through TB in 16 patients (17%) with negative SB results. Mean longest core cancer lengths were 4.6 mm for SB and 7.3 mm for TB (P < .0001). In 12 of 51 (24%) MR imaging targets with positive SB and TB results, TB led to Gleason score upgrading. In 79 MR imaging targets, positivity for cancer was 47% (n = 37) with TB-COG and 53% (n = 42) with TB-FUS (P = .16). Neither technique was superior for Gleason score assessment. Conclusion: Prebiopsy MR imaging combined with transrectal US-guided TB increases biopsy performance in detecting PCa, especially clinically significant PCa. No significant difference was observed between TB-FUS and TB-COG for TB guidance. © RSNA, 2013 Supplemental material: http://radiology.rsna.org/lookup/suppl/doi:10.1148/radiol.13121501/-/DC1.
[152]  
**TITULO / TITLE:** - Is interleukin 2 the best initial therapy for many patients with metastatic renal cell carcinoma?  
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)  
[●●Enlace al texto completo (gratuito o de pago)](1097/PPO.0b013e318292e6a2)  
**AUTORES / AUTHORS:** - Philips G; Atkins MB  
**INSTITUCIÓN / INSTITUTION:** - From the Departments of Oncology and Medicine, Georgetown Lombardi Comprehensive Cancer Center, Washington, DC.  

[153]  
**TITULO / TITLE:** - Salvage-targeted kidney cancer therapy in patients progressing on high-dose interleukin-2 immunotherapy: the UCLA experience.  
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)  
[●●Enlace al texto completo (gratuito o de pago)](1097/PPO.0b013e318292e8a4)  
**AUTORES / AUTHORS:** - Birkhauser FD; Pantuck AJ; Rampersaud EN; Wang X; Kroeger N; Pouliot F; Zomorodian N; Riss J; Li G; Kabbinavar FF; Belldegrun AS  
**INSTITUCIÓN / INSTITUTION:** - From the *Institute of Urologic Oncology, David Geffen School of Medicine, University of California, Los Angeles, CA; daggerDepartment of Urology, University of Bern, Switzerland; and double daggerDepartment of Biostatistics, School of Public Health, University of California, Los Angeles, CA.**  
**RESUMEN / SUMMARY:** - PURPOSE: To analyze the outcomes of patients with metastatic renal cell carcinoma treated with salvage-targeted therapy after progressing on high-dose interleukin (IL)-2 immunotherapy in a tertiary referral center. MATERIALS AND METHODS: A retrospective nonrandomized cohort consisting of 286 patients with metastatic renal cell carcinoma treated from 2003 to 2010 was analyzed from the University of California, Los Angeles (UCLA) Kidney Cancer database. All patients underwent cytoreductive nephrectomy, and 21 patients received salvage-targeted therapy after progression on high-dose IL-2, whereas 111 patients received targeted therapy alone. The remaining 154 patients had other treatment combinations or experimental targeted therapy agents only. Since 2003, selection of patients for high-dose IL-2 was increasingly based on clinical, pathologic, and molecular criteria (UCLA CPM criteria). Disease-specific survival was calculated from
diagnosis of metastatic renal cell carcinoma. RESULTS: Patients selected according to UCLA CPM criteria and treated with salvage-targeted therapy after progressing on high-dose IL-2 experienced a significantly greater disease-specific survival (median not reached) than those treated with targeted therapy alone (30 months; P = 0.004). Since 2006, all high-dose IL-2 patients met the UCLA CPM criteria and were able to receive salvage-targeted therapy upon progression. Disease-specific survival calculated from initiation of targeted therapy was comparable for patients treated with salvage-targeted therapy after progression on high-dose IL-2 (34 months) versus first-line targeted therapy (26 months; P = 0.175). DISCUSSION: Patients selected for high-dose IL-2 based on UCLA CPM criteria and treated with salvage-targeted therapy upon progression have achieved outstanding disease-specific survival. Our data suggest a new algorithm for carefully selected patients with metastatic renal cell carcinoma based on UCLA CPM criteria to receive first-line high-dose IL-2 while reserving their option for salvage-targeted therapy with uncompromised efficacy upon progression.

[154]

TÍTULO / TITLE: - Re: 120W greenlight high performance system laser for benign prostate hyperplasia: 68 patients with 3-year follow-up and analysis of predictors of response.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kaplan SA

[155]

TÍTULO / TITLE: - VHL gene alterations in Italian patients with isolated renal cell carcinomas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Muscarella LA; D’Agruma L; la Torre A; Gigante M; Coco M; Parrella P; Battaglia M; Carrieri G; Carella M; Zelante L; Fazio VM; Gesualdo L; Ranieri E
INSTITUCIÓN / INSTITUTION: - Laboratory of Oncology, IRCCS “Casa Sollievo della Sofferenza” Hospital, San Giovanni Rotondo, Foggia - Italy.
RESUMEN / SUMMARY: - Clear cell renal cell carcinoma (ccRCC) is the most common malignant neoplasm of the kidney and belongs to the few human
tumors known to develop from mutations of the VHL tumor suppressor gene. VHL germline mutations are associated with hereditary ccRCCs in VHL disease. However, somatic VHL gene defects may also occur in sporadic ccRCCs. In this study, we analyzed the frequency and the spectrum of VHL gene alterations in 35 Italian patients with sporadic renal cell carcinoma (RCC). Tumor-specific intragenic VHL pathogenic mutations were detected in 38% (11/29) of the ccRCC patients and 33% (2/6) of the patients with other types of RCC. One novel 18-bp in-tandem duplication and 4 previously unreported nucleotide changes in the VHL gene were described. Microsatellite analysis showed loss of heterozygosity for at least 1 informative marker in 43% (9/21) of the ccRCCs and 50% (3/6) of the non-ccRCCs; 5 of the 13 tumors (38%) harboring VHL gene alterations also had loss of heterozygosity for at least 1 microsatellite marker. Our results confirm that somatic inactivation of the VHL gene may play a pivotal role in the tumorigenesis of sporadic ccRCCs in Italian patients and suggests that mutation analysis of the VHL gene may be helpful for discriminating sporadic, VHL-gene-related ccRCCs from those related to VHL disease.

[156]

**TITULO / TITLE:** - Carbonic anhydrase IX (CAIX) is not an independent predictor of outcome in patients with clear cell renal cell carcinoma (ccRCC) after long-term follow-up.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Zhang BY; Thompson RH; Lohse CM; Dronca RS; Cheville JC; Kwon ED; Leibovich BC

**INSTITUCIÓN / INSTITUTION:** - Department of Internal Medicine, Mayo Clinic and Mayo Medical School, Rochester, MN, USA.

**RESUMEN / SUMMARY:** - OBJECTIVE: To evaluate carbonic anhydrase IX (CAIX) expression as an independent prognostic marker for clear cell renal cell carcinoma (ccRCC). With recent smaller studies showing conflicting results, we aimed to update our initial analysis in 2007 with an additional 5-year follow-up. PATIENTS AND METHODS: We provided long-term follow-up of the same cohort used in our 2007 study (730 patients with unilateral, sporadic ccRCC treated surgically between 1990 and 1999). Associations of CAIX expression with RCC death and distant metastases were evaluated using Cox proportional hazards regression models. RESULTS: CAIX was expressed in 708 (97.0%) of the specimens; 163 tumours (22.3%) had low (<=85%) expression and 567 (77.7%) high (>85%) expression. There were 483 deaths and 265 RCC-specific deaths. The median follow-up for the 247 patients still under
observation was 13.8 years. Univariately, low CAIX expression was associated with an increased risk of RCC death vs high expression (hazard ratio 1.62; P < 0.001). Low CAIX expression was not statistically significantly associated with RCC death or distant metastases after adjusting for nuclear grade or coagulative tumour necrosis. CONCLUSION: After additional long-term follow-up of our large cohort, our results continue to suggest that CAIX is not an independent prognostic marker for ccRCC.

[157] TÍTULO / TITLE: Re: (11)C-Choline PET/CT in Patients with Hormone-Resistant Prostate Cancer Showing Biochemical Relapse After Radical Prostatectomy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Taneja SS

[158] TÍTULO / TITLE: Re: prescriber monitoring for benign prostatic hyperplasia within a family medicine clinic: a comparison of medication classes.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kaplan SA

[159] TÍTULO / TITLE: Sperm-associated antigen 4, a novel hypoxia-inducible factor 1 target, regulates cytokinesis, and its expression correlates with the prognosis of renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Shoji K; Murayama T; Mimura I; Wada T; Kume H; Goto A; Ohse T; Tanaka T; Inagi R; van der Hoorn FA; Manabe I; Homma Y; Fukayama M; Sakurai T; Hasegawa T; Aburatani H; Kodama T; Nangaku M
INSTITUCIÓN / INSTITUTION: - Division of Nephrology and Endocrinology, University of Tokyo, Tokyo, Japan.
Hypoxia plays a crucial role in many pathophysiological conditions, including cancer biology, and hypoxia-inducible factor (HIF) regulates transcriptional responses under hypoxia. To elucidate the cellular responses to hypoxia, we performed chromatin immunoprecipitation with deep sequencing in combination with microarray analysis and identified HIF-1 targets. We focused on one of the novel targets, sperm-associated antigen 4 (SPAG4), whose function was unknown. SPAG4, an HIF-1-specific target, is upregulated in various cultured cells under hypoxia. Examination of SPAG4 expression using a tissue microarray consisting of 190 human renal cell carcinoma (RCC) samples revealed that SPAG4 is an independent prognostic factor of cancer-specific mortality. Live-cell imaging revealed localization of SPAG4 at the intercellular bridge in telophase. We also studied cells in which SPAG4 was knocked down. Hypoxia enhances tetraploidy, which disturbs cell proliferation, and knockdown of SPAG4 increased tetraploid formation and decreased cell proliferation under both normoxic and hypoxic conditions. Studies using deletion mutants of SPAG4 also suggested the involvement of SPAG4 in cytokinesis. Microarray analysis confirmed dysregulation of cytokinesis-related genes by knockdown of SPAG4. In conclusion, SPAG4 is an independent prognostic factor in RCC and plays a crucial role in cytokinesis to defend against hypoxia-induced tetraploid formation. This defensive mechanism may promote survival of cancer cells under hypoxic conditions, thus leading to poor prognosis.

[160]

Titulo / Title: Incidental cancer of the prostate in patients with bladder urothelial carcinoma: comprehensive analysis of 1476 radical cystoprostatectomy specimens.

Resumen / Summary: Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.05.034

Autores / Authors: Bruins HM; Djaladat H; Ahmadi H; Sherrod A; Cai J; Miranda G; Skinner EC; Daneshmand S

Institución / Institution: Urology Resident, Radboud University Nijmegen Medical Center, Department of Urology, Nijmegen, The Netherlands.

Resumen / Summary: PURPOSE: To determine the incidence, identify risk factors and determine the prognosis for incidental (clinically significant) prostate adenocarcinoma ((cs)PCA), prostatic urothelial carcinoma (PUC) and high-grade intra-epithelial neoplasia (HGPIN) in patients undergoing radical cystoprostatectomy for urothelial carcinoma of the bladder. MATERIALS AND METHODS: 1476 patients without a history of PCA were analyzed. Incidences of (cs)PCA, PUC and HGPIN were determined in the total cohort and selected
subgroups of patients. PUC was stratified in prostatic stroma (PUC-s) and prostatic urethra/duct (PUC-d) involvement. Univariate and multivariate analyses with multiple variables was performed. Recurrence-free survival (RFS) and overall survival (OS) rates were calculated. Median follow-up time was 13.2 years. RESULTS: 753 (51.0%) of the 1476 patients had cancer involving the prostate. PCA, csPCA, PUC and HGPIN were present in 37.9%, 8.3%, 21.1% and 51.2% of the patients, respectively. Of the 312 (21.1%) patients with PUC, 163 (11.0%) patients had PUC-d only and 149 (10.1%) patients PUC-s. Risk factors for csPCA, PUC and HGPIN were identified, however, absence of these risk factors did not rule out their presence. Ten-year OS in patients with no-PUC, PUC-d and PUC-s was 47.1%, 43.3% and 21.7%, respectively (p < 0.001). None of the patients with csPCA died of prostate cancer.

CONCLUSIONS: Over half of the patients undergoing radical cystoprostatectomy had cancer involving the prostate. Presence of PUC, in particular PUC-s, was associated with a worse prognosis, while csPCA did not alter survival. Pre-operative clinical and histopathologic risk factors are not reliable enough to accurately predict csPCA and/or PUC.

[161]

TÍTULO / TITLE: - Re: finasteride adherence-associated factors in chinese benign prostatic hyperplasia patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Kaplan SA

[162]

TÍTULO / TITLE: - Cell-free plasma DNA as biochemical biomarker for the diagnosis and follow-up of prostate cancer patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Wroclawski ML; Serpa-Neto A; Fonseca FL; Castro-Neves-Neto O; Pompeo AS; Machado MT; Pompeo AC; Del Giglio A
INSTITUCIÓN / INSTITUTION: - Albert Einstein Jewish Hospital, Sao Paulo, Brazil, mwroclawski@terra.com.br.
RESUMEN / SUMMARY: - The aim of this study was to evaluate the diagnostic and potential prognostic value of cell-free plasma DNA (CF-pDNA) in patients with suspected or histologically proven prostate cancer (PCa). We included 133
men with a diagnosis of PCa and 33 controls. PCa patients had blood samples prospectively drawn every 3 months for 2 years. CF-pDNA was measured by spectrophotometry. Considering a cut-off value of 140 ng/mL of CF-pDNA the area under the curve was of 0.824(0.757-0.879 with a sensitivity = 66.2 % and a specificity = 87.9 %) and the positive and negative likelihood ratio were of 5.46 and 0.39, respectively. CF-pDNA tends to decrease slightly and return to baseline values in about a week after biopsy. There was no statistical significant correlation between CF-pDNA levels at study entry with PSA, Gleason score, stage and biochemical recurrence free survival (BRFS). However, with a mean follow-up of 13.5 months, we could observe a significant shorter BRFS for patients with at least one value above 140 ng/mL of CF-pDNA during follow-up (p = 0.048). CF-pDNA is a potentially valuable biomarker for PCa diagnosis and a potential tool for the follow-up of patients with PCa.

[163]

**TÍTULO / TITLE:** - Multiparametric MR Imaging for Detection of Clinically Significant Prostate Cancer: A Validation Cohort Study with Transperineal Template Prostate Mapping as the Reference Standard.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Radiology. 2013 Apr 5.

**AUORES / AUTHORS:** - Arumainayagam N; Ahmed HU; Moore CM; Freeman A; Allen C; Sohaib SA; Kirkham A; van der Meulen J; Emberton M

**INSTITUCIÓN / INSTITUTION:** - Division of Surgery and Interventional Sciences, University College, Charles Bell House, 67-73 Riding House St, London W1W 7EJ, England; Departments of Histopathology and Radiology, University College Hospital London, London, England; Department of Radiology, Royal Marsden Hospital London, London, England; Health Services Research Unit, London School of Hygiene and Tropical Medicine, London, England.

**RESUMEN / SUMMARY:** - Purpose: To evaluate the diagnostic performance of multiparametric (MP) magnetic resonance (MR) imaging for prostate cancer detection by using transperineal template prostate mapping (TTPM) biopsies as the reference standard and to determine the potential ability of MP MR imaging to identify clinically significant prostate cancer. Materials and Methods: Institutional review board exemption was granted by the local research ethics committee for this retrospective study. Included were 64 men (mean age, 62 years [range, 40-76]; mean prostate-specific antigen, 8.2 ng/mL [8.2 mg/L] [range, 2.1-43 ng/mL], 51 with biopsy-proved cancer and 13 suspected of having clinically significant cancer that was biopsy negative or without prior biopsy. MP MR imaging included T2-weighted, dynamic contrast-enhanced and diffusion-weighted imaging (1.5 T, pelvic phased-array coil). Three radiologists independently reviewed images and were blinded to results of biopsy. Two-by-
two tables were derived by using sectors of analysis of four quadrants, two
lobes, and one whole prostate. Primary target definition for clinically significant
disease necessary to be present within a sector of analysis on TTPM for that
sector to be deemed positive was set at Gleason score of 3+4 or more and/or
cancer core length involvement of 4 mm or more. Sensitivity, negative
predictive value, and negative likelihood ratio were calculated to determine
ability of MP MR imaging to rule out cancer. Specificity, positive predictive
value, positive likelihood ratio, accuracy (overall fraction correct), and area
under receiver operating characteristic curves were also calculated.

Results: Twenty-eight percent (71 of 256) of sectors had clinically
significant cancer by primary endpoint definition. For primary endpoint definition
(>=4 mm and/or Gleason score >=3+4), sensitivity, negative predictive value,
and negative likelihood ratios were 58%-73%, 84%-89%, and 0.3-0.5,
respectively. Specificity, positive predictive value, and positive likelihood ratios
were 71%-84%, 49%-63%, and 2.3-4.4, respectively. Area under the curve
values were 0.73-0.84.

Conclusion: Results of this study indicate that MP MR imaging has a high negative predictive value to rule out clinically significant
prostate cancer and may potentially have clinical use in diagnostic pathways of
men at risk. © RSNA, 2013

particularly in the current era of targeted therapies. OBJECTIVE: To highlight morphologic mimics of clear cell renal cell carcinoma and provide strategies to help differentiate clear cell renal cell carcinoma from other renal tumors and lesions. The role of the pathologist in guiding treatment for renal malignancies will be emphasized to stress the importance of proper tumor classification in patient management. DATA SOURCES: Published literature and personal experience. CONCLUSIONS: In challenging cases, submission of additional tissue is often an inexpensive and effective way to facilitate a correct diagnosis. If immunohistochemical stains are to be used, it is best to use a panel of markers, as no one marker is specific for a given renal tumor subtype. Selection of limited markers, based on a specific differential diagnosis, can be as useful as a large panel in reaching a definitive diagnosis. For renal tumors, both the presence and absence of immunoreactivity and the pattern of labeling (membranous, cytoplasmic, diffuse, focal) are important when interpreting the results of immunohistochemical stains.

[165]

TÍTULO / TITLE: - Image-guided method for TLD-based in vivo rectal dose verification with endorectal balloon in proton therapy for prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Hsi WC; Fagundes M; Zeidan O; Hug E; Schreuder N
INSTITUCIÓN / INSTITUTION: - ProCure Proton Therapy Center, Oklahoma City, Oklahoma 73142.

RESUMEN / SUMMARY: - Purpose: To present a practical image-guided method to position an endorectal balloon that improves in vivo thermoluminescent dosimeter (TLD) measurements of rectal doses in proton therapy for prostate cancer. Methods: TLDs were combined with endorectal balloons to measure dose at the anterior rectal wall during daily proton treatment delivery. Radiopaque metallic markers were employed as surrogates for balloon position reproducibility in rotation and translation. The markers were utilized to guide the balloon orientation during daily treatment employing orthogonal x-ray image-guided patient positioning. TLDs were placed at the 12 o’clock position on the anterior balloon surface at the midprostatic plane. Markers were placed at the 3 and 9 o’clock positions on the balloon to align it with respect to the planned orientation. The balloon rotation along its stem axis, referred to as roll, causes TLD displacement along the anterior-posterior direction. The magnitude of TLD displacement is revealed by the separation distance between markers at opposite sides of the balloon on sagittal x-ray images. Results: A total of 81 in vivo TLD measurements were performed on six patients. Eighty-three percent
of all measurements (65 TLD readings) were within +5% and -10% of the planning dose with a mean of -2.1% and a standard deviation of 3.5%. Examination of marker positions with in-room x-ray images of measured doses between -10% and -20% of the planned dose revealed a strong correlation between balloon roll and TLD displacement posteriorly from the planned position. The magnitude of the roll was confirmed by separations of 10-20 mm between the markers which could be corrected by manually adjusting the balloon position and verified by a repeat x-ray image prior to proton delivery. This approach could properly correct the balloon roll, resulting in TLD positioning within 2 mm along the anterior-posterior direction. Conclusions: Our results show that image-guided TLD-based in vivo dosimetry for rectal dose verification can be performed reliably and reproducibly for proton therapy in prostate cancer.

[166]

TÍTULO / TITLE: Sperm banking is of key importance in patients with prostate cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Salonia A; Capogrosso P; Castiglione F; Russo A; Gallina A; Ferrari M; Clementi MC; Castagna G; Briganti A; Cantiello F; Damiano R; Montorsi F
INSTITUCIÓN / INSTITUTION: Department of Urology, University Vita-Salute San Raffaele, Milan, Italy; Research Doctorate Program in Urology, Magna Graecia University, Catanzaro, Italy. Electronic address: salonia.andrea@hsr.it.
RESUMEN / SUMMARY: OBJECTIVE: To assess the need for sperm banking among patients with prostate cancer (PCa) who are candidates for radical prostatectomy (RP). DESIGN: Cross-sectional study. SETTING: Urologic department. PATIENT(S): Cohort of 510 Caucasian-European candidates for RP. INTERVENTION(S): A 10-item self-administered questionnaire to assess opinions on sperm banking before RP, to which descriptive statistics and logistic regression models were applied. MAIN OUTCOME MEASURE(S): PCa patients’ wishes for preoperative sperm banking. RESULT(S): Data collection was completed for 495 patients (97.1%). Ninety-nine (20%) expressed a wish for preoperative sperm banking. Men who wanted to bank sperm were younger (mean 62.2 vs. 65.1 years), were more frequently childless (21.2% vs. 8.8%), and more frequently had a more intense desire for fatherhood (64.7% vs. 9.3%) than the patients not interested in banking sperm. Willingness to bank sperm was not affected by the patient’s educational or relationship status. Moreover,
the interest for sperm banking was maintained regardless of cost issues. Overall, 84% of the patients considered it necessary to have a dedicated service of preoperative sperm cryopreservation. CONCLUSION(S): One out of five PCa patients would bank sperm before RP. Most patients considered it necessary to establish a dedicated service for preoperative sperm cryopreservation, regardless of their own motivation to bank sperm.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Haddad BR; Gu L; Mirtti T; Dagvadorj A; Vogiatzi P; Hoang DT; Bajaj R; Leiby B; Ellsworth E; Blackmon S; Ruiz C; Curtis M; Fortina P; Ertel A; Liu C; Rui H; Visakorpi T; Bubendorf L; Lallas CD; Trabulsi EJ; McCue P; Gomella L; Nevalainen MT
INSTITUCIÓN / INSTITUTION: - Department of Oncology, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, District of Columbia.
RESUMEN / SUMMARY: - The molecular mechanisms underlying progression of prostate cancer (PCa) to castrate-resistant (CR) and metastatic disease are poorly understood. Our previous mechanistic work shows that inhibition of transcription factor Stat5 by multiple alternative methods induces extensive rapid apoptotic death of Stat5-positive PCa cells in vitro and inhibits PCa xenograft tumor growth in nude mice. Furthermore, STAT5A/B induces invasive behavior of PCa cells in vitro and in vivo, suggesting involvement of STAT5A/B in PCa progression. Nuclear STAT5A/B protein levels are increased in high-grade PCs, CR PCs, and distant metastases, and high nuclear STAT5A/B expression predicts early disease recurrence and PCa-specific death in clinical PCas. Based on these findings, STAT5A/B represents a therapeutic target protein for advanced PCa. The mechanisms underlying increased Stat5 protein levels in PCa are unclear. Herein, we demonstrate amplification at the STAT5A/B gene locus in a significant fraction of clinical PCa specimens. STAT5A/B gene amplification was more frequently found in PCas of high histologic grades and in CR distant metastases. Quantitative in situ analysis revealed that STAT5A/B gene amplification was associated with increased STAT5A/B protein expression in PCa. Functional studies showed that increased STAT5A/B copy numbers conferred growth advantage in PCa cells in vitro and
as xenograft tumors in vivo. The work presented herein provides the first evidence of somatic STAT5A/B gene amplification in clinical PCas.

[168] TÍTULO / TITLE: - Side effects of perioperative intravesical treatment and treatment strategies for these side effects.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Griffin JG; Holzbeierlein J
INSTITUCIÓN / INSTITUTION: - Department of Urology, University of Kansas Medical Center, Kansas City, KS 66160, USA. jgriffin3@kumc.edu

RESUMEN / SUMMARY: - Perioperative intravesical chemotherapy has a well-established role in the treatment of non-muscle invasive bladder cancer. There are multiple agents that can be used in this fashion with varying properties. Although chemical cystitis is the most common side effect and is usually self-limiting, significant toxicity can occur with intravesical chemotherapy. It is imperative that the urologist is aware of the acute and delayed side effects of intravesical chemotherapy and how to manage potential complications. Both local and systemic toxicities are discussed, as well as strategies to minimize and manage them.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Shelbaia A; Elsaied WM; Elghamrawy H; Abdullah A; Salaheldin M
INSTITUCIÓN / INSTITUTION: - Department of Urology, Cairo University Hospitals, Cairo, Egypt. Electronic address: ahmedshelbaia2007@hotmail.com.
RESUMEN / SUMMARY: - OBJECTIVE: To study the effect selective of alpha-blocker (tamsulosin HCl) on erectile function in married male patients who are suspected to have benign prostatic hyperplasia (BPH). MATERIALS AND METHODS: Our study was a prospective randomized single blinded study in one-to-one fashion conducted upon 60 patients, all of them married, between
May 2010 and May 2011, the patients under the study were attending the outpatient clinic of the New Kasr Al-Aini Teaching Hospital and Students Hospital, Cairo University, complaining of lower urinary tract symptoms (LUTS) either obstructive, irritative, or both and erectile dysfunction (ED). History was taken from all patients; all patients were examined by digital rectal examination and abdominal examination. We performed pelvic ultrasound, serum prostatic-specific antigen (PSA) measurements, other routine investigations, and uroflowmetry. Assessment of sexual function changes was by the International Index of Erectile Function (IIEF) and penile Doppler ultrasound. RESULTS: In the tamsulosin group, a significant statistical improvement was detected in the erectile function score and intercourse satisfaction score with significant improvement in total IIEF beside the improvement in the International Prostatic Symptom Score (IPSS). Although orgasmic function score showed significant worsening. CONCLUSION: Tamsulosin HCl capsules showed a significant statistical improvement in the erectile function, sexual desire, and intercourse satisfaction score with significant improvement in total IIEF in patients with lower urinary tract symptoms because of benign prostatic hyperplasia.

[170] TÍTULO / TITLE: - Inverse association between body mass index and chronic kidney disease in older diabetic adults.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kao YM; Chen JD
INSTITUCIÓN / INSTITUTION: - Department of Family Medicine, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan.
RESUMEN / SUMMARY: - PURPOSE: To identify associations among body mass index (BMI), diabetes, and chronic kidney disease (CKD) in older adults in Taiwan. METHODS: This study enrolled 3334 participants aged 65 years and above who underwent an annual health screening at a medical center from January 2006 to December 2010. CKD was defined as an estimated glomerular filtration rate less than 60 mL/min/1.73 m(2). A multiple logistic regression analysis was used to determine associations among BMI, diabetes, and CKD. RESULTS: The prevalence rate of CKD was 19.7% and 10.5% in diabetic and nondiabetic subjects, respectively. A multivariate model indicated that age, diabetes, hypertriglyceridemia, low levels of high-density lipoprotein cholesterol, and hyperuricemia were associated with an increased risk of CKD. Furthermore, there was an inverse association between BMI and CKD in older diabetic patients, with odds ratios of 3.71, 2.32, 2.12, and 1.31 in underweight,
normal, overweight, and obese subjects, respectively, compared with nondiabetic subjects of normal weight. CONCLUSIONS: There was an inverse association between BMI and CKD in older diabetic patients but no such association was found in nondiabetic older adults. More attention should be given to older underweight diabetic patients because they have a higher risk of CKD.
RESUMEN / SUMMARY: - PURPOSE: To report long-term outcomes of low- and intermediate-risk prostate cancer patients treated with high-dose hypofractionated radiation therapy (HypoRT). METHODS AND MATERIALS: Patients with low- and intermediate-risk prostate cancer were treated using 3-dimensional conformal radiation therapy to a dose of 66 Gy in 22 daily fractions of 3 Gy without hormonal therapy. A uniform 7-mm margin was created around the prostate for the planning target volume, and treatment was prescribed to the isocenter. Treatment was delivered using daily ultrasound image-guided radiation therapy. Common Terminology Criteria for Adverse Events, version 3.0, was used to prospectively score toxicity. Biochemical failure was defined as the nadir prostate-specific antigen level plus 2 ng/mL. RESULTS: A total of 129 patients were treated between November 2002 and December 2005. With a median follow-up of 90 months, the 5- and 8-year actuarial biochemical control rates were 97% and 92%, respectively. The 5- and 8-year actuarial overall survival rates were 92% and 88%, respectively. Only 1 patient died from prostate cancer at 92 months after treatment, giving an 8-year actuarial cancer-specific survival of 98%. Radiation therapy was well tolerated, with 57% of patients not experiencing any acute gastrointestinal (GI) or genitourinary (GU) toxicity. For late toxicity, the worst grade >/=2 rate for GI and GU toxicity was 27% and 33%, respectively. There was no grade >3 toxicity. At last follow-up, the rate of grade >/=2 for both GI and GU toxicity was only 1.5%. CONCLUSIONS: Hypofractionation with 66 Gy in 22 fractions prescribed to the isocenter using 3-dimensional conformal radiation therapy produces excellent biochemical control rates, with moderate toxicity. However, this regimen cannot be extrapolated to the intensity modulated radiation therapy technique.
BACKGROUND: Anti-tumor vaccination is a new frontier in cancer treatment applicable to immunogenic neoplasms such as prostate and renal cancers. GX301 is a vaccine constituted by four telomerase peptides and two adjuvants, Montanide ISA-51 and Imiquimod. OBJECTIVE: The aim of this study was to analyze safety and tolerability of GX301 in an open-label, phase I/II trial. Immunological and clinical responses were also evaluated as secondary endpoints. EXPERIMENTAL DESIGN: GX301 was administered by intradermally injecting 500 μg of each peptide (dissolved in Montanide ISA-51) in the skin of the abdomen. Imiquimod was applied as a cream at the injection sites. The protocol included 8 administrations at days 1, 3, 5, 7, 14, 21, 35, 63. Eligible patients were affected with stage IV prostate or renal cancer resistant to conventional treatments. Patients were clinically and immunologically monitored up to 6 months from the first immunization.

RESULTS: No grade 3-4 adverse events were observed. Evidence of vaccine-specific immunological responses was detected in 100% of patients. Disease stabilization occurred in 4 patients. Prolonged progression-free survival and overall survival were observed in patients showing a full pattern of vaccine-specific immunological responses. CONCLUSION: GX301 demonstrated to be safe and highly immunogenic. Further studies are needed to determine its clinical efficacy.

[175]

TÍTULO / TITLE: The inhibition of p85alphaPI3KSer83 phosphorylation prevents cell proliferation and invasion in prostate cancer cells.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Feola A; Cimini A; Migliucci F; Iorio R; Zucchegna C; Rothenberger R; Cito L; Porcellini A; Unteregger G; Tombolini V; Giordano A; Di Domenico M

INSTITUCIÓN / INSTITUTION: Department of Biochemistry, Biophysics and General Pathology, Second University of Naples, Italy.

RESUMEN / SUMMARY: Phosphoinositide 3-kinase proteins are composed by a catalytic p110 subunit and a regulatory p85 subunit. There are three classes of PI3K, named class I, II and III, on the bases of the protein domain constituting and determining their specificity. The first one is the best characterized and includes a number of key elements for the integration of different cellular signals. Regulatory p85 subunit shares with the catalytic p110 subunit, a N-terminal SH3 domain showing homology with the protein domain Rho-GTP-ase. After cell stimulation, all class I PI3Ks are recruited to the inner face of the
plasma membrane, where they generate phosphatidylinositol-3,4,5-trisphosphate by direct phosphorylation of phosphatidylinositol-4,5-bisphosphate. All pathways trigger the control of different phenomena such as cell growth, proliferation, apoptosis, adhesion and migration through various downstream effectors. We have previously provided direct evidences that a Serine in position 83, adjacent to the N-terminal SH3 domain of regulatory subunit of PI3K, is a substrate of PKA. The aim of this work is to confirm the role of p85alphaPI3KSer83 in regulating cell proliferation, migration and invasion in prostate cancer cells LNCaP. To this purpose cells were transfected with mutant forms of p85, where Serine was replaced by Alanine, where phosphorylation is prevented, or Aspartic Acid, to mimic the phosphorylated residue. The findings of this study suggest that identifying a peptide mimicking the sequence adjacent to Ser 83 may be used to produce antibodies against this residue that can be proposed as useful tool for prognosis by correlating phosphorylation at Ser83 with tumor stage. J. Cell. Biochem. © 2013 Wiley Periodicals, Inc.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
- Enlace al texto completo (gratuito o de pago) 1200/JCO.2012.45.4959
AUTORES / AUTHORS: - Wudhikarn K; Colling CW; Robinson RA; Vaena DA
INSTITUCIÓN / INSTITUTION: - University of Iowa, Iowa City Veterans Affairs Medical Center, 601 Hwy 6W, Rm 6W29, Iowa City, IA 52246; daniel-vaena@uiowa.edu.

[177] TÍTULO / TITLE: - Frequency of computed tomography examinations in the follow-up care of testicular cancer patients - an evaluation of patterns of care in Germany.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
- Enlace al texto completo (gratuito o de pago) 1159/000349952
AUTORES / AUTHORS: - Rusner C; Stang A; Dieckmann KP; Friedel H
INSTITUCIÓN / INSTITUTION: - Institut fur Klinische Epidemiologie, Medizinische Fakultat, Martin-Luther-Universitat Halle-Wittenberg, Halle, Germany. carsten.rusner@medizin.uni-halle.de
BACKGROUND: Exposure to radiation resulting from diagnostic imaging procedures probably increases late cancer risk. Patterns of care regarding the application of computed tomography (CT) imaging in testicular cancer patients were investigated. METHODS: The database of a large German health insurance company comprising 850,000 insured men was searched for cases of testicular cancer arising in the years 2005 and 2006. The number of CT scans applied during a 3-year period of follow-up was noted for each individual patient and the resulting cumulative radiation dose was estimated. The number of CT scans actually observed was compared to guideline recommendations. RESULTS: 177 patients were identified. Within the 3-year observation period, patients received a mean of 4.4 CT scans (standard error: 0.4) whereas a number of 6.2 would have been expected according to contemporary guidelines. Patients were exposed to an estimated total median diagnostic radiation dose of 30 millisieverts (mSv) (interquartile range: 10-54 mSv). CONCLUSION: There is a considerable gap between recommendation and actual performance regarding the number of CT scans applied to testicular cancer patients. Unfamiliarity of clinicians with guidelines as well as poor acceptance of high numbers of CT scans scheduled may have contributed to create this particular pattern of care.

[178]

ETS transcription factor ESE1/ELF3 orchestrates a positive feedback loop that constitutively activates NF-κB and drives prostate cancer progression.

Chromosomal translocations leading to deregulated expression of ETS transcription factors are frequent in prostate tumors. Here, we report a novel mechanism leading to oncogenic activation of the ETS factor ESE1/ELF3 in prostate tumors. ESE1/ELF3 was overexpressed in human primary and metastatic tumors. It mediated transforming phenotypes in vitro and in vivo and induced an inflammatory transcriptome with changes in relevant oncogenic pathways. ESE1/ELF3 was induced by IL-1beta through NF-kappaB and was a crucial mediator of the phenotypic and transcriptional changes induced by IL-1beta in prostate cancer cells. This linkage was mediated by...
interaction of ESE1/ELF3 with the NF-kappaB subunits p65 and p50, acting by enhancing their nuclear translocation and transcriptional activity and by inducing p50 transcription. Supporting these findings, gene expression profiling revealed an enrichment of NF-kappaB effector functions in prostate cancer cells or tumors expressing high levels of ESE1/ELF3. We observed concordant upregulation of ESE1/ELF3 and NF-kappaB in human prostate tumors that was associated with adverse prognosis. Collectively, our results define an important new mechanistic link between inflammatory signaling and the progression of prostate cancer.

[179]

TÍTULO / TITLE: - Effect of small angiokinase inhibitor nintedanib (BIBF 1120) on QT interval in patients with previously untreated, advanced renal cell cancer in an open-label, phase II study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Invest New Drugs. 2013 Apr 27.
●●Enlace al texto completo (gratis o de pago) 1007/s10637-013-9962-7
AUTORES / AUTHORS: - Eisen T; Shparyk Y; Macleod N; Jones R; Wallenstein G; Temple G; Khder Y; Dallinger C; Studeny M; Loembe AB; Bondarenko I
INSTITUCIÓN / INSTITUTION: - Cambridge University Health Partners, Addenbrooke’s Hospital, Cambridge, CB2 0QQ, UK, tgge2@cam.ac.uk.
RESUMEN / SUMMARY: - Purpose Some targeted anticancer agents are associated with serious ventricular tachyarrhythmias, which may be predicted by electrocardiographic evaluation of drug-related QT prolongation. We studied the effects of nintedanib (BIBF 1120; an oral, triple angiokinase inhibitor targeting vascular endothelial growth factor, fibroblast growth factor, and platelet-derived growth factor receptors) on the QT interval in patients with renal cell carcinoma (RCC) participating in an open-label phase II trial. Methods Treatment-naive, adult patients with unresectable/metastatic, clear cell RCC received nintedanib 200 mg twice daily. QT intervals were evaluated at baseline (day -1), on day 1 (after the first dose), and on day 15 (steady state) by 12-lead electrocardiograms (ECGs) performed in triplicate. Pharmacokinetic sampling was also undertaken. Results Among 64 evaluable patients, the upper limits of the 2-sided 90 % confidence intervals for the adjusted mean time-matched changes in QTcF interval (corrected for heart rate by Fridericia’s method) from baseline to day 1 and 15 (primary ECG endpoint) were well below the regulatory threshold of 10 ms at all times. No relationship between nintedanib exposure and change from baseline in QTcF was seen. Nintedanib was generally well tolerated with no drug-related cardiovascular adverse events. Conclusion Nintedanib administered at 200 mg twice daily was not associated with clinically relevant QT prolongation.
The interval to biochemical failure is prognostic for metastasis, prostate cancer-specific mortality, and overall mortality after salvage radiation therapy for prostate cancer.

**RESUMEN / SUMMARY:**

Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:**


**AUTORES / AUTHORS:**

Johnson S; Jackson W; Li D; Song Y; Foster C; Foster B; Zhou J; Vainshtein J; Feng F; Hamstra D

**INSTITUCIÓN / INSTITUTION:**

Department of Radiation Oncology, The University of Michigan Medical Center, Ann Arbor, Michigan. Electronic address: Skylerjohn3101@gmail.com.

**RESUMEN / SUMMARY:**

PURPOSE: To investigate the utility of the interval to biochemical failure (IBF) after salvage radiation therapy (SRT) after radical prostatectomy (RP) for prostate cancer as a surrogate endpoint for distant metastasis (DM), prostate cancer-specific mortality (PCSM), and overall mortality (OM).

METHODS AND MATERIALS: A retrospective analysis of 575 patients treated with SRT after RP from a single institution. Of those, 250 patients experienced biochemical failure (BF), with the IBF defined as the time from commencement of SRT to BF. The IBF was evaluated by Kaplan-Meier and Cox proportional hazards models for its association with DM, PCSM, and OM.

RESULTS: The median follow-up time was 85 (interquartile range [IQR] 49.8-121.1) months, with a median IBF of 16.8 (IQR, 8.5-37.1) months. With a cutoff time of 18 months, as previously used, 129 (52%) of patients had IBF </=18 months. There were no differences among any clinical or pathologic features between those with IBF </= and those with IBF >18 months. On log-rank analysis, IBF </=18 months was prognostic for increased DM (P<.0001, HR 4.9, 95% CI 3.2-7.4), PCSM (P<.0001, HR 4.1, 95% CI 2.4-7.1), and OM (P<.0001, HR 2.7, 95% CI 1.7-4.1). Cox proportional hazards models with adjustment for other clinical variables demonstrated that IBF was independently prognostic for DM (P<.001, HR 4.9), PCSM (P<.0001, HR 4.0), and OM (P<.0001, HR 2.7). IBF showed minimal change in performance regardless of androgen deprivation therapy (ADT) use.

CONCLUSION: After SRT, a short IBF can be used for early identification of patients who are most likely to experience progression to DM, PCSM, and OM. IBF </=18 months may be useful in clinical practice or as an endpoint for clinical trials.
TÍTULO / TITLE: Secondary debulking surgery in ovarian cancer patients with isolated nodal recurrence located in the region above and behind the renal vein.

RESUMEN / SUMMARY: OBJECTIVE: We describe our early experience with a suprarenal and retrorenal para-aortic lymphadenectomy involving the mobilization of the left kidney. METHODS: Three patients with isolated nodal recurrence located in the region above and behind the renal vein underwent the removal of these metastatic lymph nodes using a left renal mobilization procedure. RESULTS AND CONCLUSION: The enlarged suprarenal and retrorenal lymph nodes were safely and effectively removed in all 3 patients. Postoperatively, a lymphatic fistula developed in one patient. However, no morbidities related to renal mobilization, including renal ischemia, were observed in the current series. A further large, prospective study is required to evaluate this surgical procedure.

[182] - CASTELLANO -

TÍTULO / TITLE: Vigilancia activa en cancer de prostata de bajo riesgo. Aceptacion por el paciente y resultados.

TÍTULO / TITLE: Active Surveillance in Low-Risk Prostate Cancer. Patient Acceptance and Results.

RESUMEN / SUMMARY: OBJECTIVES: To evaluate the acceptance of active monitoring by patients treated in our healthcare community and to report the clinical results of an active surveillance program in patients with low-risk
prostate cancer. MATERIAL AND METHODS: Prospective study of patients enrolled in an active surveillance programme at our centre between 2004 and 2012. The inclusion criteria were PSA <10ng/ml, Gleason score <=6, clinical stage T1c/T2a, <=2 positive cores, and no more than 50% of the core being affected. Curative treatment was proposed when faced with pathological progression over the course of the monitoring. RESULTS: In 2011, only 17% of the total number of potential candidate patients rejected their inclusion in a surveillance programme and were treated actively. We analysed a series of 144 patients included in our active surveillance protocol. The mean follow-up time was 3.22 years (SD 2.08). A total of 110 patients (76.3%) remained under active monitoring, with an estimated median treatment-free survival after diagnosis of 6.9 years (95% CI: 6.2-7.6). The percentage of patients who remained free of treatment at 2 and 5 years was 96.3% (95% CI: 92.8%-99.8%) and 70.9% (95% CI: 59.3%-85.5%), respectively. Thirty four patients (23.6%) required curative treatment. The mean time to treatment was 4.6 years (SD 2.3). CONCLUSIONS: Active surveillance of highly selected patients with low-risk prostate cancer is a valid alternative therapy that is accepted by patients in our community.

[183]

TÍTULO / TITLE: - Prognostic value of CXCR4 expression in patients with clear cell renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Li G; Badin G; Zhao A; Gentil-Perret A; Tostain J; Peoc'h M; Gigante M
INSTITUCIÓN / INSTITUTION: - Department of Urology, North Hospital, CHU Saint-Etienne, University of Jean-Monnet, Saint-Etienne, France. grli2001@yahoo.fr.
RESUMEN / SUMMARY: - Introduction: The expression of CXCR4 is implicated in the metastatic dissemination of different cancers. The information on its prognostic value has been very limited in clear cell renal cell carcinoma (ccRCC). Our objective was to explore the prognostic value of CXCR4 in ccRCC. Materials and methods: 104 patients with a ccRCC were studied. There were 69 men and 35 women with an average age of 64.5 years old (range: 34-86 years). The CXCR4 expression was evaluated by immunohistochemistry. The follow-up varied from 12 to 184 months with a mean of 79.5 months. Kaplan-Meier with a log rank test was performed to compare overall survival and cancer-specific survival after surgery. Univariate and multivariate analyses were performed according to the Cox regression model. Results: CXCR4 expression was found in 68/104 (65.4%) of tumor samples. CXCR4 expression was located in the nucleus in 55/68 (80.8%) cases while cytoplasm or membrane location was found in 13/68 (19.2%) cases. High expression was
found in 25/68 (36.8%) cases. During follow-up, 39 patients died, of which 26 died of cancer. Kaplan-Meier analysis revealed that a high expression of CXCR4 was associated with a reduced overall survival (p=0.017) and cancer-specific survival (p=0.022). Univariate analysis indicated that a high expression of CXCR4 was a significant factor for a poorer overall survival (p=0.020) and cancer-specific survival (p=0.027). By multivariate analysis, a high expression of CXCR4 appeared to be an independent factor of overall survival (p=0.024) and cancer-specific survival (p=0.028). Conclusion: This study suggested that a high CXCR4 expression was correlated with a worse outcome for ccRCC patients.

[184]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Kwon H; Kang HC; Lee JH

INSTITUCIÓN / INSTITUTION: - Department of Family Medicine, Yonsei University College of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - OBJECTIVE: To investigate the association between the metabolic syndrome (MetS) and the predictors of the progression of benign prostatic hyperplasia (BPH). MATERIALS AND METHODS: A total of 778 male police officers in their 50s with moderate to severe lower urinary tract symptoms (International Prostate Symptom Score > 7) were included in the present study. We defined the predictors of the risk of clinical progression of BPH as the total prostate volume >/=31 cm(3), prostate-specific antigen level >/=1.6 ng/mL, maximal flow rate <10.6 mL/s, and postvoid residual urine volume of >/=39 mL. The MetS was defined using the National Cholesterol Education Program-Adult Treatment Panel III guidelines. We used the Mantel-Haenszel extension test and logistic regression analyses to statistically examine their relationship. RESULTS: The percentage of participants with >/=1 predictor for the progression of BPH, the percentage of participants with a total prostate volume of >/=31 cm(3), and the percentage of participants with a postvoid residual urine volume of >/=39 mL increased significantly with the increase in the number of components of the MetS (P = .003, P = .001, and P = .007, respectively). After adjusting for age and serum testosterone levels, the MetS was shown to be significantly associated with the presence >/=1 predictor for the progression of BPH (odds ratio 1.423, 95% confidence interval 1.020-1.986). CONCLUSION: Our data have shown that the MetS is associated with the predictors of the risk
of clinical progression of BPH in men in their 50s with moderate to severe lower urinary tract symptoms.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
□□ Enlace al texto completo (gratuito o de pago) 10.1016/j.juro.2013.03.003
AUTORES / AUTHORS: - Wood DP; Penson DP

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
□□ Enlace al texto completo (gratuito o de pago) 1111/hepr.12156
AUTORES / AUTHORS: - Ishii T; Hatano E; Taura K; Mizuno T; Kawai T; Fukudo M; Katsura T; Uemoto S
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Graduate School of Medicine Kyoto University, Kyoto, Japan.
RESUMEN / SUMMARY: - The efficacy of sorafenib against hepatocellular carcinoma (HCC) has been extensively reported. However, there is little information available about the use of sorafenib for HCC patients with end-stage renal failure. We herein report the safe introduction of sorafenib therapy for a HCC patient on hemodialysis. A 63-year-old man had received multidisciplinary treatments, including transarterial chemoembolization (TACE) and radiofrequency ablation, for HCC since 1996, and had been undergoing hemodialysis since 2005. He also underwent TACE for multiple liver recurrence of HCC in 2011. Sorafenib therapy (200 mg/day) started 8 days after the TACE. The pharmacokinetic parameters of sorafenib and its active metabolite, M-2, were within the reference levels observed in patients with normal renal function 8 and 9 days after the initiation of sorafenib. The dose of sorafenib was reduced to 200 mg every other day on day 154 due to hypertension and general fatigue. Because of the progression of disease after 5 months, sorafenib was withdrawn on day 180. He was admitted to the emergency department because of a high fever during hemodialysis on day 201, and died of septic shock induced by Staphylococcus lugdunensis on day 203. Sorafenib was well tolerated at an initial dose of 200 mg/day for a HCC patient undergoing
hemodialysis, thus indicating that renal failure is not necessarily a contraindication for sorafenib therapy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1093/ndt/gft008
AUTORES / AUTHORS: - Lalowski M; Magni F; Mainini V; Monogioudi E; Gotsopoulos A; Soliymani R; Chinello C; Baumann M
INSTITUCIÓN / INSTITUTION: - Meilahti Clinical Proteomics Core Facility, Biochemistry and Developmental Biology, Institute of Biomedicine, University of Helsinki, Helsinki, Finland.
RESUMEN / SUMMARY: - Matrix-assisted laser desorption ionization (MALDI)-profiling and imaging mass spectrometry are promising technologies for measuring hundreds of different molecules directly on tissues. For instance, small molecules, drugs and their metabolites, endogenous lipids, carbohydrates and complex peptides/proteins can be measured at the same time without significant disruption of sample integrity. In this review, the potential of MALDI-profiling/imaging technologies in disease proteomics, drug action and studies of cellular processes in the context of kidney tissue is described. Spatial and sequence information obtained in tissue MALDI-profiling/imaging studies can be correlated with other mass spectrometry-based techniques, auxiliary imaging technologies and routine (immuno) histochemical staining.

[188] TÍTULO / TITLE: - Androgens and estrogens stimulate ribosome biogenesis in prostate and breast cancer cells in receptor dependent manner.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.gene.2013.04.018
AUTORES / AUTHORS: - Ray S; Johnston R; Campbell DC; Nugent S; McDade SS; Waugh D; Panov KI
INSTITUCIÓN / INSTITUTION: - School of Biological Sciences, The Queen’s University Belfast, Belfast BT9 7BL, UK.
RESUMEN / SUMMARY: - Ribosome biogenesis is a fundamental cellular process intimately linked to cell growth and proliferation, which is upregulated in most of cancers especially in aggressive cancers. In breast and prostate cancers steroid hormone receptor signalling is the principal stimulus for cancer growth
and progression. Here we investigated the link between estrogen and androgen receptor signalling and the initial stage of ribosome biogenesis - transcription of rRNA genes. We have discovered that oestrogen or androgen treatment can positively regulate rRNA synthesis in breast and prostate cancer cells respectively and that this effect is receptor dependent. This novel and interesting finding suggests a previously unidentified link between steroid hormone receptor signalling pathways and the regulation of ribosome biogenesis.

[189]

**TÍTULO / TITLE:** Impact of lymphovascular invasion on oncological outcomes in patients with upper tract urothelial carcinoma after radical nephroureterectomy.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Hurel S; Roupret M; Ouzzane A; Rozet F; Xylinas E; Zerbib M; Berod AA; Ruffion A; Adam E; Cussenot O; Houlgatte A; Phe V; Nouhaud FX; Bensadoun H; Delage F; Guillotreau J; Guy L; Karsenty G; De La Taille A; Colin P

**INSTITUCIÓN / INSTITUTION:** Department of Urology, Cote de Nacre Hospital, CHU Caen, Caen.

**RESUMEN / SUMMARY:** OBJECTIVES: To assess the impact of lymphovascular invasion (LVI) on upper urinary tract urothelial carcinomas (UTUCs) in a multicentre study on cancer-specific survival (CSS), recurrence-free survival and metastasis-free survival (MFS). To show the negative impact of LVI for patients with pN0/x disease and to stratify these patients into risk groups for metastatic relapse. PATIENTS AND METHODS: A multicentre retrospective study was performed on patients who underwent radical nephroureterectomy between 1995 and 2010. LVI status was evaluated as a prognostic factor for survival using univariate and multivariate Cox regression analysis. RESULTS: Overall, 551 patients were included and were divided into two groups: those without LVI (LVI-), n = 388 and those with LVI (LVI+), n = 163. LVI+ status was associated with high stage and grade UTUC and lymph node metastasis (P < 0.001). The 5-year CSS and MFS rates were significantly worse in the LVI+ group than in LVI- group (52.2 vs 84.5%, P < 0.001 and 43.8 vs 82.7%, P < 0.001, respectively). In multivariate analysis, LVI+ status was an independent prognostic factor for CSS and MFS (P = 0.04 and P < 0.001). These findings were confirmed for the pN0/x patient subgroup (n = 504, P < 0.001). In the pN0/x patient subgroup, we described a prognostic tool for MFS based on independent factors that permitted us to stratify patients into groups of high, intermediate or low risk of metastasis relapse. CONCLUSIONS: The presence
of LVI was a strong predictor of a poor outcome for UTUC. When a lymphadenectomy has not been achieved, the report of LVI status is crucial to identify those patients at higher risk for metastatic relapse.

[190]

**Título / Title:** Transglutaminase 2 inhibition found to induce p53 mediated apoptosis in renal cell carcinoma.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary

**Revista / Journal:** FASEB J. 2013 May 23.

**Autores / Authors:** Ku BM; Kim DS; Kim KH; Yoo BC; Kim SH; Gong YD; Kim SY

**Institución / Institution:** *Cancer Cell and Molecular Biology Branch, Division of Cancer Biology, and daggerColorectal Cancer Branch, Division of Translational and Clinical Research I, Research Institute, National Cancer Center, Goyang, Korea; and.

**Resumen / Summary:** Renal cell carcinoma (RCC), the predominant form of kidney cancer, is characterized by high resistance to radiation and chemotherapy. This study shows that expression of protein cross-linking enzyme transglutaminase 2 (TGase 2) is markedly increased in 7 renal cell carcinoma (RCC) cell lines in comparison to HEK293 and other cancer cell lines, such as NCI 60. However, the key role of TGase 2 in RCC was not clear. The down-regulation of TGase 2 was found to stabilize p53 expression, thereby inducing a 3- to 10-fold increase in apoptosis for 786-O, A498, CAKI-1, and ACHN cell lines by DAPI staining. MEF cells from TGase 2−/− mice showed stabilized p53 under apoptotic stress to compare to MEFs from wild-type mice. TGase 2 directly cross links the DNA binding domain of p53, leading to p53 depletion via autophagy in RCC. TGase 2 and p53 expression showed an inverse relationship in RCC cells. This finding implies that induced expression of TGase 2 promotes tumor cell survival through p53 depletion in RCC.-Ku, B.M., Kim, D.-S. Kim, K.-H., Yoo, B.C., Kim, S.-H., Gong, Y.-D., Kim, S.-Y.

Transglutaminase 2 inhibition found to induce p53 mediated apoptosis in renal cell carcinoma.

[191]

**Título / Title:** Differences in prostate cancer detection rates according to the level of glomerular filtration rate in patients with prostate specific antigen levels of 4.0-10.0 ng/ml.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary

Aims: To investigate differences in prostate cancer detection rates according to the level of glomerular filtration rates (GFR).

Materials and methods: Patients with prostate-specific antigen (PSA) levels of 4.0 - 10.0 ng/ml were analysed. Age, serum creatinine, estimated GFR, body mass index, total PSA (tPSA), free PSA (fPSA), per cent free PSA (%fPSA), comorbidities, biopsy Gleason sum and per cent positive core were retrospectively reviewed. All parameters were compared to show whether patients with GFR < 60 ml/min/1.73 m(2) (group A) have higher risk of prostate cancer than patients with GFR >/= 60 (group B). The primary endpoint was cancer detection rate and the secondary endpoints were differences in mean tPSA, fPSA, %fPSA and pathologic outcomes. Results: A total of 1092 men (243 cancer patients) were included. Mean age was 65.8 +/- 7.7 years. No differences in mean age and tPSA were found between groups A and B. Mean fPSA, %fPSA and cancer detection rate were significantly higher in group A than group B. The incidence of %fPSA < 25% was significantly lower in group A than in group B. GFR < 60 ml/min/1.73 m(2), fPSA and %fPSA < 25% were significant predictors for the presence of prostate cancer in patients with tPSA between 4 and 10 ng/ml. However, %fPSA < 25% was not a significant predictor for group A. Conclusions: Because of the increased cancer detection rates in patients with CKD of stage >/= 3 whose tPSA levels are 4.0 - 10.0 ng/ml, performing prostate biopsy should be actively considered in patients with CKD.

[192]

TÍTULO / TITLE: Hypoxia upregulates the gene expression of mitochondrial aconitase in prostate carcinoma cells.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Tsui KH; Chung LC; Wang SW; Feng TH; Chang PL; Juang HH

INSTITUCIÓN / INSTITUTION: K Tsui, Urology, Chang Gung Memorial Hospital, Kwie-Shan, Taiwan.

RESUMEN / SUMMARY: Hypoxia induces metabolic alternation in cancer cells by stabilizing hypoxia inducible factor 1-alpha (HIF-1alpha), which regulates the bioenergetic genes of glycolysis and lipid metabolic pathways. However, the target genes of hypoxia induced metabolic alteration in the prostate remain
Mitochondrial aconitase (mACON) is an enzyme that is central to carbohydrate and energy metabolism and is responsible for the interconversion of citrate to isocitrate as part of the citric acid cycle in the human prostate. We evaluated the effects of the molecular mechanisms of hypoxia on mACON gene expression in PC-3 and LNCaP human prostate carcinoma cells. Immunoblotting assays revealed that hypoxia modulated mACON and lactate dehydrogenase A (LDHA) protein expression, while these effects were attenuated when HIF-1alpha was knocked down. Hypoxia induced fatty acid synthase (FASN) in PC-3 cells while hypoxia blocked FASN gene expression in LNCaP cells after 24 h incubation. Results of real-time RT-qPCR, immunoblotting, and transient gene expression assays revealed that hypoxia treatment or co-transfection with HIF-1alpha expression vector enhanced gene expression of mACON, implying that hypoxia modulated mACON at the transcriptional level. Hypoxia-induced mACON promoter activity is dependent on the DNA fragment located at -1013 to -842 upstream of the translation initiation site. L-mimosine, an iron chelator, stabilized HIF-1alpha but downregulated mACON gene expression suggesting that iron chelation blocked the hypoxia-induced mACON gene expression. These results suggest that hypoxia dysregulates the expressions of LDHA, FASN, and mACON genes; and the hypoxia-induced mACON gene expression is via the HIF-1alpha-dependent and iron-dependent pathways in prostate carcinoma cells.

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[193]

**TÍTULO / TITLE:** - Re: A phase 3, double-blind, randomised, parallel-group, placebo-controlled study of oral weekly alendronate for the prevention of androgen deprivation bone loss in nonmetastatic prostate cancer: the cancer and osteoporosis research with alendronate and leuprolide (CORAL) study.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


  ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.01.075

**AUTORES / AUTHORS:** - Taneja SS

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[194]

**TÍTULO / TITLE:** - Re: effectiveness of a combination therapy using calcineurin inhibitor and mTOR inhibitor in preventing allograft rejection and post-transplantation renal cancer progression.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


  ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2012.12.036
AUTORES / AUTHORS: - Atala A

TÍTULO / TITLE: - Decision Regret in Men Undergoing Dose-Escalated Radiation Therapy for Prostate Cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Steer AN; Aherne NJ; Gorzynska K; Hoffman M; Last A; Hill J; Shakespeare TP

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, North Coast Cancer Institute, University of New South Wales, Coffs Harbour, Australia.

RESUMEN / SUMMARY: - PURPOSE: Decision regret (DR) is a negative emotion associated with medical treatment decisions, and it is an important patient-centered outcome after therapy for localized prostate cancer. DR has been found to occur in up to 53% of patients treated for localized prostate cancer, and it may vary depending on treatment modality. DR after modern dose-escalated radiation therapy (DE-RT) has not been investigated previously, to our knowledge. Our primary aim was to evaluate DR in a cohort of patients treated with DE-RT.

METHODS AND MATERIALS: We surveyed 257 consecutive patients with localized prostate cancer who had previously received DE-RT, by means of a validated questionnaire. RESULTS: There were 220 responses (85.6% response rate). Image-guided intensity modulated radiation therapy was given in 85.0% of patients and 3-dimensional conformal radiation therapy in 15.0%. Doses received included 73.8 Gy (34.5% patients), 74 Gy (53.6%), and 76 Gy (10.9%). Neoadjuvant androgen deprivation (AD) was given in 51.8% of patients and both neoadjuvant and adjuvant AD in 34.5%. The median follow-up time was 23 months (range, 12-67 months). In all, 3.8% of patients expressed DR for their choice of treatment. When asked whether they would choose DE-RT or AD again, only 0.5% probably or definitely would not choose DE-RT again, compared with 8.4% for AD (P<.01). CONCLUSION: Few patients treated with modern DE-RT express DR, with regret appearing to be lower than in previously published reports of patients treated with radical prostatectomy or older radiation therapy techniques. Patients experienced more regret with the AD component of treatment than with the radiation therapy component, with implications for informed consent. Further research should investigate regret associated with individual components of modern therapy, including AD, radiation therapy and surgery.
**TÍTULO / TITLE:** Androgen Receptor Roles in the Development of Benign Prostate Hyperplasia.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Izumi K; Mizokami A; Lin WJ; Lai KP; Chang C

**INSTITUCIÓN / INSTITUTION:** George H. Whipple Laboratory for Cancer Research, University of Rochester Medical Center, Rochester, New York; Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York; Department of Integrative Cancer Therapy and Urology, Kanazawa University, Kanazawa, Japan; Department of Urology, University of Rochester Medical Center, Rochester, New York; Department of Radiation Oncology (Wilmot Cancer Center), University of Rochester Medical Center, Rochester, New York.

**RESUMEN / SUMMARY:** Benign prostate hyperplasia (BPH) is a major cause of lower urinary tract symptoms, with an increased volume of transitional zone and associated with increased stromal cells. It is known that androgen/androgen receptor (AR) signaling plays a key role in development of BPH, and that blockade of this signaling decreases BPH volume and can relieve lower urinary tract symptoms, but the mechanisms of androgen/AR signaling in BPH development remain unclear, and the effectiveness of current drugs for treating BPH is still limited. The detailed mechanisms of androgen/AR signaling need to be clarified, and new therapies are needed for better treatment of BPH patients. This review focuses on roles of AR in epithelial and stromal cells in BPH development. In epithelial cells, AR may contribute to BPH development via epithelial cell-stromal cell interaction with alterations of epithelial-mesenchymal transition, leading to proliferation of stromal cells. Data from several mouse models with selective knockout of AR in stromal smooth-muscle cells and/or fibroblasts indicate that the AR in stromal cells can also promote BPH development. In prostatic inflammation, AR roles in infiltrating macrophages and epithelial and stromal cells have been linked to BPH development, which has led to discovery of new therapeutic targets. For example, targeting AR with the novel AR degradation enhancer, ASC-J9 offers a potential therapeutic approach against BPH development.

[197]

**TÍTULO / TITLE:** Induction of retinol-binding protein 4 and placenta-specific 8 expression in human prostate cancer cells remaining in bone following osteolytic tumor growth inhibition by osteoprotegerin.

148
New drugs that inhibit the osteoprotegerin (OPG)/receptor activator of NF-kappaB ligand (RANKL)/RANK pathway have demonstrated efficacy for the treatment of bone metastasis. Toxicities induced by these drugs, however, including osteonecrosis of the jaw and hypocalcemia, may adversely affect therapy. The aim of this study was to identify additional therapeutic targets that can be combined with OPG/RANKL/RANK pathway inhibition in the treatment of prostate cancer bone metastasis. We established a stable transfectant that produces high levels of OPG mRNA and protein from PC-3 human prostate cancer cells (PC3-OPG). The culture medium of PC3-OPG cells significantly inhibited the differentiation of mouse monocytes into mature osteoclasts. Furthermore, when PC3-OPG cells were injected into the bones of nude mice, bone destruction and tumor-induced osteoclast formation were reduced. Injection into bone of the mixtures containing equal amounts of green fluorescent protein (GFP)-expressing PC-3 cells (PC3-GFP) and PC3-OPG cells also reduced bone destruction, compared to the control mixture. PC3-GFP cells were subsequently isolated from bone tumors and used for microarray analysis to assess changes in gene expression following osteolytic tumor growth inhibition by OPG. We selected the top 10 upregulated genes based on results from microarrays and confirmed mRNA expression of each gene by RT-PCR. The expression patterns of retinol-binding protein 4 (RBP4) and placenta-specific 8 (PLAC8) were consistent with microarray results. Expression of these genes was also increased in the bone tumors of PC3-GFP/PC3-OPG-injected mice. Knockdown of both RBP4 and PLAC8 by siRNA inhibited the growth of PC-3 cells in vitro. Thus, RBP4 and PLAC8 may become new therapeutic targets for prostate cancer bone metastasis, in combination with OPG/RANKL/RANK pathway inhibition.
TARGETED THERAPIES HAVE SHOWN PROFOUND EFFECTS ON THE OUTCOME OF PATIENTS WITH ADVANCED RENAL CELL CARCINOMA (RCC). HOWEVER, THE OPTIMAL TREATMENT FOR RCC OF NON-CLEAR CELL HISTOLOGY (nccRCC)-TYPICALLY EXCLUDED FROM TRIALS OF TARGETED AGENTS-REMAINS UNCERTAIN.

MATERIALS AND METHODS: By carrying out extensive searches of PubMed and ASCO databases, we identified and summarised research into the biological characteristics, clinical behaviour and treatment of different histological subtypes of nccRCC, focusing on targeted therapy. RESULTS: The available data suggest that treatments currently approved for RCC are active in ncc subtypes, although the overall clinical benefit may be less than for clear cell RCC. Temsirolimus has proven benefit over interferon-alfa (IFN-alpha) in patients with nccRCC, based on phase III data, while everolimus, sunitinib and sorafenib have all demonstrated some degree of activity in nccRCC in expanded-access trials. No clear picture has emerged of whether individual histological subtypes are particularly responsive to any individual treatment. CONCLUSIONS: Further molecular studies into the pathogenesis of RCC histological subtypes will help direct the development of novel, appropriate targeted agents. Clinical trials specifically designed to evaluate the role of targeted agents in nccRCC are ongoing, and data from trials with sunitinib and everolimus will be reported soon.

[199]

Racial differences in time from prostate cancer diagnosis to treatment initiation: A Population-Based Study.

BACKGROUND: Timely delivery of care has been identified by the Institute of Medicine as an indicator for quality health care, and treatment delay is a potentially modifiable obstacle that can contribute to the disparities among African American (AA) and Caucasian patients in prostate cancer recurrence and mortality. Using the Surveillance, Epidemiologic and End Results (SEER)-Medicare linked database, we compared time from diagnosis to treatment in AA and Caucasian prostate cancer patients. METHODS: A total of 2506 AA and 21,454 Caucasian patients diagnosed with localized prostate cancer from 2004 through 2007 and treated within 12 months were included.
Linear regression was used to assess potential differences in time to treatment between AA and Caucasian patients, after adjusting for sociodemographic and clinical covariates. RESULTS: Time from diagnosis to definitive (prostatectomy and radiation) treatment was longer for AA patients in all risk groups, and most pronounced in high-risk cancer (96 versus 105 days, P < .001). On multivariate analysis, racial differences to any and definitive treatment persisted (beta = 7.3 and 7.6, respectively, for AA patients). Delay to definitive treatment was longer in high-risk (versus low-risk) disease and in more recent years.

CONCLUSIONS: AA patients with prostate cancer experienced longer time from diagnosis to treatment than Caucasian patients with prostate cancer. AA patients appear to experience disparities across all aspects of this disease process, and together these factors in receipt of care plausibly contribute to the observed differences in rates of recurrence and mortality among AA and Caucasian patients with prostate cancer. Cancer 2013. Esta es una cita bibliográfica que va por delante de la publicación en papel. La fecha indicada en la cita provista, NO corresponde con la fecha o la cita bibliográfica de la publicación en papel. La cita bibliográfica definitiva (con el volumen y su paginación) saldrá en 1 ó 2 meses a partir de la fecha de la emisión electrónica-online. *** This is a bibliographic record ahead of the paper publication. The given date in the bibliographic record does not correspond to the date or the bibliographic citation on the paper publication. The publisher will provide the final bibliographic citation (with the volume, and pagination) within 1 or 2 months from the date the record was published online. © 2013 American Cancer Society.

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[200]
TÍTULO / TITLE: - O-GlcNAc transferase integrates metabolic pathways to regulate the stability of c-MYC in human prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Itkonen HM; Minner S; Guldvik IJ; Sandmann MJ; Tsourlakis MC; Berge V; Svindland A; Schlomm T; Mills IG
INSTITUCIÓN / INSTITUTION: - Centre for Molecular Medicine Norway, University of Oslo.
RESUMEN / SUMMARY: - Tumorigenesis is characterised by changes in transcriptional regulation and the androgen receptor (AR) has been identified as a key driver in prostate cancer. In this study, we show that the hexosamine biosynthetic pathway (HBP) genes are overexpressed in clinical prostate cancer and androgen-regulated in cell-lines. HBP senses metabolic status of the cell and produces an essential substrate for O-GlcNAc transferase (OGT), which
regulates target proteins via glycosylation. Using immunohistochemistry, we found that OGT is up-regulated in the protein level in prostate cancer (n=1987) and its expression correlates with high Gleason Score (GS), pT and pN stages and biochemical recurrence (for all, p<0.0001). Both a small molecule inhibitor and siRNAs targeting OGT decreased prostate cancer cell growth. Microarray profiling revealed that the principal effects of the OGT inhibitor in prostate cancer cells are on cell cycle progression and DNA replication. We identified MYC as a candidate upstream regulator of these genes and found that OGT inhibitor caused a dose-dependent loss of c-MYC protein but not mRNA in cell lines. Finally, we observed a statistically significant co-expression between c-MYC and OGT in human prostate cancer samples (n=1306, p=0.0012).

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[201]

TÍTULO / TITLE: - Haptoglobin proved a prognostic biomarker in peripheral blood of patients with personalized Peptide vaccinations for advanced castration-resistant prostate cancer.
RESUMEN / SUMMARY: - Haptoglobin (Hp) is a well-known acute-phase protein that possibly has influence on tumors through the immune response. This study was conducted to evaluate the correlation between Hp expression and the effect of treatment by cancer peptide vaccines in advanced castration-resistant prostate cancer (CRPC) patients. Hp expression was measured by RT-PCR using peripheral blood mononuclear cells (PBMCs) collected from advanced CRPC patients, who were divided into two groups: long-term survivors and short-term survivors. Before cancer peptide vaccination (pre-vaccination), Hp expression was almost same in the two groups, but after cancer peptide vaccination (post-vaccination), Hp expression was higher in short-term survivors, suggesting that Hp expression in the PBMCs increased in short-term survivors after treatment by cancer peptide vaccines. Our results suggest that Hp expression level in the PBMCs can serve as a prognostic biomarker in treatment by cancer peptide vaccine in advanced CRPC patients.

AUTORES / AUTHORS: - Pang X; Tashiro K; Eguchi R; Komatsu N; Sasada T; Itoh K; Kuhara S
INSTITUCIÓN / INSTITUTION: - Graduate School of Systems Life Sciences, Kyushu University.

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[202]
TÍTULO / TITLE: - Deposition of the lectin pathway of complement in renal biopsies of lupus nephritis patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Nishihara RM; Magrini F; Mocelin V; Messias-Reason IJ

INSTITUCIÓN / INSTITUTION: - Laboratory of Molecular Immunopathology and Department of Medical Pathology, Federal University of Parana, Curitiba, Brazil; Positivo University, Medicine Department, Curitiba, Brazil.

RESUMEN / SUMMARY: - BACKGROUND/AIMS: Lupus nephritis (LN) is one of the most serious manifestations of SLE occurring in 66-90% of these patients. The complement system is part of the innate immunity and modulator of inflammation and the adaptative immune response. Mannan-binding lectin (MBL) and Ficolin-2 (FCN-2) are important members of the lectin pathway of complement activation. Despite the significant participation of complement in the pathogenesis of the LN, there are few reports demonstrating “in situ” deposition of complement components in renal biopsy specimens in this disorder. The present study investigated the deposition of complement components in kidney specimens of LN patients. METHODS: Renal biopsies of 11 patients with SLE and LN were evaluated for immunofluorescence staining for IgG, IgA, IgM, C3, and C1q. Additionally, MBL, FCN-2 and C5b-9 were researched using monoclonal antibodies. RESULTS: All the biopsies were positive for IgG, C3, and C1q, eight were positive IgM and five had IgA deposition in glomerular tissue. The terminal complex of complement C5b9 was positive in all cases, MBL in nine (82%) cases; seven (63.6%) of them presenting concomitantly FCN-2 deposition. Patients presenting MBL deposition had higher mean of urinary proteins (9.0g/day) than patients with negative MBL deposition (mean of 2.3g/day). CONCLUSIONS: In this study, we demonstrated in situ the participation of complement in the renal injury, including MBL and FCN-2 of the lectin pathway; also the strong role of C5b-9 in the pathogenesis of LN.

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TÍTULO / TITLE: - Does 4-tert-octylphenol affect estrogen signaling pathways in bank vole Leydig cells and tumor mouse Leydig cells in vitro?

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Kotula-Balak M; Chojnacka K; Hejmej A; Galas J; Satola M; Bilinska B
RESUMEN / SUMMARY: - Primary Leydig cells obtained from bank vole testes and the established tumor Leydig cell line (MA-10) have been used to explore the effects of 4-tert-octylphenol (OP). Leydig cells were treated with two concentrations of OP (10^-4M, 10^-8M) alone or concomitantly with anti-estrogen ICI 182,780 (1μM). In OP-treated bank vole Leydig cells, inhomogeneous staining of estrogen receptor alpha (ERalpha) within cell nuclei was found, whereas it was of various intensity among MA-10 Leydig cells. The expression of ERalpha mRNA and protein decreased in both primary and immortalized Leydig cells independently of OP dose. ICI partially reversed these effects at mRNA level while at protein level abrogation was found only in vole cells. Dissimilar action of OP on cAMP and androgen production was also observed. This study provides further evidence that OP shows estrogenic properties acting on Leydig cells. However, its effect is diverse depending on the cellular origin.

[204]

TÍTULO / TITLE: - Percutaneous cryoablation of renal tumours: outcomes from 171 tumours in 147 patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
         ● Enlace al texto completo (gratuito o de pago) 1111/bju.12122
AUTORES / AUTHORS: - Breen DJ; Bryant TJ; Abbas A; Shepherd B; McGill N; Anderson JA; Lockyer RC; Hayes MC; George SL
INSTITUCIÓN / INSTITUTION: - Department of Radiology, University Hospitals of Southampton NHS Foundation Trust, Southampton, UK.
RESUMEN / SUMMARY: - OBJECTIVE: To evaluate the technical and oncological efficacy of an image-guided cryoablation programme for renal tumours.
PATIENTS AND METHODS: A prospective analysis of technical and radiological outcomes was undertaken after treatment of 171 consecutive tumours in 147 patients. Oncological efficacy in a subset of 125 tumours in 104 patients with >6 months' radiological follow-up and a further subset of 62 patients with solitary, biopsy-proven renal carcinoma was also analysed.
Factors influencing technical success, as determined by imaging follow-up, and complication rates were statistically analysed using a statistics software package and logistic regression analyses. RESULTS: No variables were found to predict subtotal treatment, although gender (P = 0.08), tumour size of >4 cm (P = 0.09) and central location of tumour (P = 0.07) approached significance. Upper pole location was the single variable that was found to predict complications (P = 0.006). Among the 104 patients (125 tumours), radiologically
assessed at $\geq 6$ months and with a mean radiological follow-up of 20.1 months, we found a single case of unexpected late local recurrence.

CONCLUSION: Percutaneous image-guided cryoablation, at a mean of 20.1 months’ follow-up, appears to provide a safe and effective treatment option with a low complication rate. Anteriorly sited tumours should not be considered a contraindication for percutaneous image-guided cryoablation.

[205]

TÍTULO / TITLE: - Effect of dutasteride on clinical progression of benign prostatic hyperplasia in asymptomatic men with enlarged prostate: a post hoc analysis of the REDUCE study.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Toren P; Margel D; Kulkarni G; Finelli A; Zlotta A; Fleshner N

INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Surgery, University of Toronto, University Health Network, 610 University Avenue, 3-130, Toronto, Ontario, Canada M5G 2M9.

RESUMEN / SUMMARY: - OBJECTIVE: To assess the role of dutasteride in preventing clinical progression of benign prostatic hyperplasia in asymptomatic men with larger prostates. DESIGN: Post hoc analysis of four year, double blind Reduction by Dutasteride of Prostate Cancer Events (REDUCE) study PARTICIPANTS: 1617 men randomised to dutasteride or placebo with a prostate size $>40$ mL and baseline International Prostate Symptom Score (IPSS) $<8$. Subjects who took medications for benign prostatic hyperplasia were excluded at study entry. INTERVENTIONS: Placebo or dutasteride 0.5 mg daily. MAIN OUTCOME MEASURES: Comparison of risk of clinical progression of benign prostatic hyperplasia at four years (defined as a $\geq 4$ point worsening on IPSS, acute urinary retention, urinary tract infection, or surgery related to benign prostatic hyperplasia). RESULTS: 825 participants took placebo, 792 took dutasteride. A total of 464 (29%) experienced clinical progression benign prostatic hyperplasia, 297 (36%) taking placebo, 167 (21%) taking dutasteride ($P<0.001$). The relative risk reduction was 41% and the absolute risk reduction 15%, with a number needed to treat (NNT) of 7. Among men who had acute urinary retention and surgery related to benign prostatic hyperplasia, the absolute risk reduction for dutasteride was 6.0% and 3.8%, respectively. On multivariable regression analysis adjusting for covariates, dutasteride significantly reduced clinical progression of benign prostatic hyperplasia with an odds ratio of 0.47 (95% CI 0.37 to 0.59, $P<0.001$). Analysis of time to first event yielded a hazard ratio of 0.673 ($P<0.001$) for those taking dutasteride. Sexual adverse events were most common and similar to prior reports. LIMITATIONS: Further prospective studies may be warranted to demonstrate generalisability of
these results. CONCLUSIONS: This study is the first to explore the benefit of treating asymptomatic or mildly symptomatic men with an enlarged prostate. Dutasteride significantly decreased the incidence of benign prostatic hyperplasia clinical progression.

[206]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

[207]
TITULO / TITLE: - A novel p53 mutant found in iatrogenic urothelial cancers is dysfunctional and can be rescued by a second-site global suppressor mutation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
have therapeutic benefit. N131Y is likely to contribute directly to tumour phenotype and is a promising candidate biomarker of AA exposure and disease. Rare mutations thus do not necessarily point to sites where amino acid exchanges are phenotypically neutral. Encounter with mutagenic insults targeting cryptic sites can reveal specific signature hotspots.

[208]

**TÍTULO / TITLE:** - Prognostic impact of LDH levels in patients with relapsed/refractory seminoma.

**RESUMEN / SUMMARY:** - Ver link al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - J Cancer Res Clin Oncol. 2013 May 3.

**AUTORES / AUTHORS:** - Powles T; Bascoul-Mollevi C; Kramar A; Lorch A; Beyer J

**INSTITUCIÓN / INSTITUTION:** - St. Bartholomew’s Hospital, Charterhouse Square, London, EC1A7BE, UK.

**RESUMEN / SUMMARY:** - PURPOSE: To evaluate the impact of age and LDH levels in patients with relapsed seminoma. METHODS: Data on the 204 seminoma from the International Prognostic Factor Study Group (IPFSG) were analyzed. All patients experienced unequivocal relapse/progression after at least three cisplatin-based chemotherapy cycles. Age and LDH at relapse were assessed in addition to previously identified prognostic factors for all germ cell tumor patients from the database (J Clin Oncol 28:4906, 2010). RESULTS: The impact of the IPFSG score remained highly significant in multivariate analysis. In addition, LDH >/=1.5 times the upper limit of normal (ULN) was significant in univariate (HR 1.96; CI 1.06-3.61) and multivariate analysis (HR 1.90; CI 1.00-3.62). Age, however, was not significant. Therefore, LDH was incorporated into a modified new IPFSG seminoma score by moving patients to the next unfavorable group for patients with LDH values >/=1.5 x ULN. Three prognostic groups were thus generated, which better subdivided seminoma patients than the original IPFSG score. Progression-free survival at 2 years: “very low risk” (n = 23) 85.7 % (95 % CI 62-95), “low risk” (n = 44) 62.7 % (95 % CI 46-75) and “intermediate risk” (n = 36) 35.1 % (95 % CI 20-51). Overall survival at 3 years: “very low risk” 88.8 % (95 % CI 62-97), “low risk” 71.3 % (95 % CI 55-83) and “intermediate risk” 51.3 % (95 % CI 33-67). CONCLUSION: The addition of LDH, but not age, improves the impact of the IPFSG prognostic score in seminoma patients relapsing or progressing after cisplatin-based chemotherapy.

[209]
Título / Title: Phase 1 prospective evaluation of the oncological adequacy of robotic assisted video-endoscopic inguinal lymphadenectomy in patients with penile carcinoma.

Resumen / Summary: A video-endoscopic (laparoscopic and robotic) approach has been proposed as a less morbid procedure in several retrospective studies. To date, none has evaluated the oncological adequacy with regard to whether all relevant nodes have been removed. To the authors’ knowledge this is the first prospective study of a robotic or laparoscopic inguinal lymphadenectomy that evaluates the oncological adequacy of this approach for penile cancer. The study shows that robotic inguinal lymphadenectomy allowed adequate staging of disease in the inguinal region by removing all relevant lymph nodes as assessed by an independent evaluating urological oncologist.

Objetivo: To prospectively determine the oncological adequacy of robotic assisted video-endoscopic inguinal lymphadenectomy (RAVEIL).

Patients and Methods: Patients with T1-3N0 penile cancer were enrolled into a prospective phase I trial at a tertiary care institution from March 2010 to January 2012. All patients underwent an initial RAVEIL approach. Verification of adequacy of dissection was performed by an independent surgeon via a separate open incision at the conclusion of the RAVEIL procedure. Out of 10 patients, if more than two superficial inguinal fields with >/=2 nodes or more than four with >/=1 node remained within the superficial dissection field, the study would not proceed to phase II. Results: Of 10 enrolled patients two had inguinal metastases and all positive nodes were detected by RAVEIL. The remaining eight patients had no metastases, with a mean of nine (range 5-21) left and nine (range 6-17) right nodes removed. One inguinal field RAVEIL was converted to an open dissection. The verifying surgeon confirmed that 18 of 19 inguinal fields (94.7% in nine patients) had an adequate dissection. Two benign nodes were found just beneath Scarpa’s fascia above the inguinal dissection field. Limitations of the study include an inability to determine decisively what specific wound complications were related to RAVEIL because of the protocol-specified creation of a small inguinal incision for verification of adequate...
dissection. CONCLUSION: RAVEIL allowed adequate staging of disease in the inguinal region among patients with penile cancer at risk for inguinal metastases.

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[210] TÍTULO / TITLE: - Phase 1 prospective evaluation of the oncological adequacy of robotic assisted video-endoscopic inguinal lymphadenectomy in patients with penile carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Ornellas AA
INSTITUCIÓN / INSTITUTION: - Hospital Mario Kroeff, RJ, Brazil; Department of Urology, Brazilian National Cancer Institute, RJ, Brazil.

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RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Kovtun IV; Cheville JC; Murphy SJ; Johnson SH; Zarei S; Kosari F; Sukov WR; Karnes RJ; Vasmatis G
INSTITUCIÓN / INSTITUTION: - Authors’ Affiliations: Departments of Molecular Pharmacology and Experimental Therapeutics, Laboratory Medicine and Pathology, Molecular Medicine, and Urology, Mayo Clinic, Rochester, Minnesota.
RESUMEN / SUMMARY: - Gleason score 7 (GS7) prostate cancer [tumors with both Gleason patterns 3 (GP3) and 4 (GP4)] portends a significantly more aggressive tumor than Gleason score 6 (GS6). It is, therefore, critical to understand the molecular relationship of adjacent GP3 and GP4 tumor cell populations and relate molecular abnormalities to disease progression. To decipher molecular relatedness, we used laser capture microdissection (LCM) and whole-genome amplification (WGA) to separately collect and amplify DNA from adjacent GP3 and GP4 cell populations from 14 cases of GS7 prostate cancer. We then carried out massively parallel mate-pair next generation sequencing (NGS) to examine the landscape of large chromosomal alterations.
We identified four to 115 DNA breakpoints in GP3 and 17 to 480 in GP4. Our findings indicate that while GP3 and GP4 from the same tumor each possess unique breakpoints, they also share identical ones, indicating a common origin. Approximately 300 chromosomal breakpoints were localized to the regions affected in at least two tumors, whereas more than 3,000 were unique within the set of 14 tumors. TMPRSS2-ERG was the most recurrent rearrangement present in eight cases, in both GP3 and GP4. PTEN rearrangements were found in five of eight TMPRSS2-ERG fusion-positive cases in both GP3 and GP4. Hierarchical clustering analysis revealed that GP3 has greater breakpoint similarity to its partner GP4 compared with GP3 from different patients. We show evidence that LCM, WGA, and NGS of adjacent tumor regions provide an important tool in deciphering lineage relationships and discovering chromosomal alterations associated with tumor progression. Cancer Res; 73(11); 3275-84. ©2013 AACR.

[212] TÍTULO / TITLE: - FGFR1 is Essential for Prostate Cancer Progression and Metastasis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Yang F; Zhang Y; Ressler SJ; Ittmann MM; Ayala GE; Dang TD; Wang F; Rowley DR
INSTITUCIÓN / INSTITUTION: - Molecular and Cellular Biology, Baylor College of Medicine.
RESUMEN / SUMMARY: - The fibroblast growth factor receptor FGFR1 is ectopically expressed in prostate carcinoma cells, but its functional contributions are undefined. In this study, we report the evaluation of a tissue-specific conditional deletion mutant generated in an ARR2PBi(Pbsn) Cre/TRAMP/fgfr1loxP/loxP transgenic mouse model of prostate cancer. Mice lacking fgfr1 in prostate cells developed smaller tumors that also included distinct cancer foci still expressing fgfr1 indicating focal escape from gene excision. Tumors with confirmed fgfr1 deletion exhibited increased foci of early, well-differentiated cancer and phyllodes-type tumors, and tumors that escaped fgfr1 deletion primarily exhibited a poorly differentiated phenotype. Consistent with these phenotypes, mice carrying the fgfr1 null allele survived significantly longer than those without fgfr1 deletion. Most interestingly, all metastases were primarily negative for the fgfr1 null allele, exhibited high FgfR1 expression and a neuroendocrine phenotype regardless of fgfr1 status in the primary tumors. Together, these results suggest a critical and permissive role of ectopic FGFR1
signaling in prostate tumorigenesis and particularly in mechanisms of metastasis.

[213]
**TITULO / TITLE:** - Hypermethylation of TWIST1 and NID2 in Tumor Tissues and Voided Urine in Urinary Bladder Cancer Patients.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**REVISTA / JOURNAL:** - DNA Cell Biol. 2013 May 19.
**AUTORES / AUTHORS:** - Yegin Z; Gunes S; Buyukalpelli R
**INSTITUCIÓN / INSTITUTION:** - 1 Department of Medical Biology, Ondokuz Mayis University, Samsun, Turkey.
**RESUMEN / SUMMARY:** - Bladder cancer like other cancers arises from the accumulation of many genetic and epigenetic changes that lead to the activation of proto-oncogenes or inactivation of tumor suppressor genes. We aimed to investigate the methylation patterns of Twist homolog 1 (TWIST1) and nidogen-2 (NID2) genes in bladder cancer. Fifty six histologically confirmed bladder tumor samples and paired 24 urine samples constituted the study group and was compared with 15 age- and gender-matched noncancerous individuals. DNA was purified from both tumor and urine samples. The methylation status of the two genes was analyzed by methylation-specific polymerase chain reaction (MSP) in both urinary bladder cell carcinoma samples and urine samples. Sensitivity and specificity values of the method were assessed and compared with the results of the cytology test. Methylation of TWIST1 and NID2 was detected in 98.2% and 96.4% of the tumor samples, and in 87.5% and 95.8% of the urine samples, respectively. The sensitivity of TWIST1 and NID2 genes (87.5% and 95.8% in urine samples, respectively), was higher compared with urine cytology (62.5%) for cancer detection. The sensitivity of any of the two genes was 88.8% (8/9) for low-grade cases. The sensitivity of urine cytology was 33.3% for the same low-grade cases. To be used in the early noninvasive diagnosis of bladder cancer, the combined methylation analysis of TWIST1 and NID2 genes may be a simple, noninvasive, sensitive, and specific method for detecting cancer cells in urine.

[214]
**TITULO / TITLE:** - Outcomes of transperineal template-guided prostate biopsy in 409 patients.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
WHAT'S KNOWN ON THE SUBJECT? AND WHAT DOES THE STUDY ADD?: With an aging population and routine use of PSA testing, there is an increase in men undergoing biopsy to assess for prostate cancer. The most common route for accessing the prostate is through the rectum, which potentially exposes the patient to otherwise innocuous Enterobacteriaceae. The rising incidence of extended-spectrum beta-lactamase has been linked to a rise in post-TRUS biopsy infection rates internationally. The study describes an alternative route for biopsy of the prostate that is associated with a very low infection rate, whilst still maintaining a good tumour detection rate.

OBJECTIVE: To present the template-guided transperineal prostate biopsy (TPB) outcomes for patients of two urologists from a single institution.

PATIENTS AND METHODS: We conducted a prospective study of 409 consecutive men who underwent TPB between December 2006 and June 2008 in a tertiary referral centre using a standardized 14-region technique. The procedure was performed as day surgery under general anaesthesia with fluoroquinolone antibiotic cover. Follow-up took place within 2 weeks, during which time men were interviewed using a standardized template. Results were compared with those of the Australian national prostate biopsy audits performed by the Urological Society of Australia and New Zealand (USANZ).

RESULTS: Indications for biopsy included elevated prostate-specific antigen (PSA) level (75%), with a median PSA level of 6.5 ng/mL, abnormal digital rectal examination (8%) and active surveillance (AS) re-staging (18%). The mean patient age was 63 years and two-thirds of patients were undergoing their first biopsy. A positive biopsy was found in 232 men, 74% of whom had a Gleason score of >/=7. The overall cancer detection rate was 56.7% (USANZ 2005 national audit = 56.5%). Stratified between those having their first TPB or a repeat procedure (after a previous negative biopsy), the detection rates were 64.4 and 35.6%, respectively. Significantly higher detection rates were found in prostates <50 mL in volume than in larger prostates (65.2 vs 38.3%, respectively, P < 0.001). Haematuria was the most common side effect (51.7%). Others included dysuria (16.4%), acute urinary retention (4.2%) and fever (3.2%). One patient (0.2%) had septicaemia requiring i.v. antibiotics. Repeat biopsy was not associated with increased complication rates.

CONCLUSIONS: TPB is a safe and efficacious technique, with a cancer detection rate of 56.7% in the present series, and a low incidence of major side effects. Stratified by prostate volume, the detection rate of TPB was higher in smaller glands. Given
the relatively low rate of serious complications, clinicians could consider increasing the number of TPB biopsy cores in larger prostates as a strategy to improve cancer detection within this group. Conversely, in patients on AS programmes, a staging TPB may be a superior approach for patients undergoing repeat biopsy so as to minimize their risk of serious infection.

[215]
TÍTULO / TITLE: - Prognostic significance of Bcl-xL expression and efficacy of Bcl-xL targeting therapy in urothelial carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Yoshimine S; Kikuchi E; Kosaka T; Mikami S; Miyajima A; Okada Y; Oya M
INSTITUCIÓN / INSTITUTION: - Department of Urology, Keio University School of Medicine, Tokyo, Japan.
RESUMEN / SUMMARY: - Background:Bcl-xL has an important role in the control of cell death through its inhibition of apoptosis. The aim of this study was to investigate the clinicopathological significance of Bcl-xL in upper urinary tract urothelial carcinoma (UTUC) and the therapeutic effect of targeting Bcl-xL protein in urothelial carcinoma (UC) cells.Methods:We evaluated the immunohistochemical expression of Bcl-xL in 175 UTUC patients to determine the clinical role of Bcl-xL expression in clinical outcome. We used bafilomycin A1 (BMA) as a specific inhibitor of Bcl-xL to examine the biological effects in UC cells in vitro and in vivo.Results:Immunohistochemical analysis of Bcl-xL expression revealed that patients with a high Bcl-xL score had a significantly lower 5-year cancer-specific survival (CSS) rate (53.2%) than those with a low Bcl-xL score (77.2%) (P=0.0011). Multivariate analysis indicated that a high Bcl-xL score was an independent prognostic factor of CSS (P=0.023). BMA inhibited UMUC-3 cell proliferation in vitro by induction of apoptosis. Treatment with BMA significantly inhibited tumour growth in UMUC-3 tumours in this mouse xenograft model accompanied by an elevated apoptosis induction.Conclusion:Bcl-xL appears to be a significant molecular marker for the prognosis of UTUCs. Targeting Bcl-xL may be a promising therapeutic strategy for patients with UC.British Journal of Cancer advance online publication, 14 May 2013; doi:10.1038/bjc.2013.216 www.bjcancer.com.

[216]
TÍTULO / TITLE: - An analysis of patients with T2 renal cell carcinoma (RCC) according to tumour size: a population-based analysis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

163
OBJECTIVE: To examine the discriminant properties of the most contemporary version of the Tumour-Node-Metastasis (TNM) staging for renal cell carcinoma (RCC) sub-classification of T2 lesions according to a threshold size of 10 cm. Other thresholds were also assessed. PATIENTS AND METHODS: Between 1988 and 2006, within the Surveillance, Epidemiology, and End Results database, patients with T2 N0-2 M0-1 RCC treated with a nephrectomy were abstracted. Tumour size was evaluated according to several thresholds: >/=8, >/=9, >/=10, >/=11, and >/=12 cm. Kaplan-Meier and life tables for cancer-specific mortality (CSM) were computed. Several Cox regression models were fitted for prediction of CSM, using different thresholds. The predictive accuracy of various thresholds was compared using the area under the curve and methods of calibration. RESULTS: In all, 4963 patients were identified. Kaplan-Meier analyses showed statistically significant CSM-free survival differences between all examined thresholds. In multivariable Cox regression models, all tested tumour size thresholds emerged as independent predictors of CSM. Of all thresholds, the values of 9 (0.55) and 11 cm (0.55) achieved the highest discrimination in univariable analysis, followed by 10 (0.539), 12 (0.539), and 8 cm (0.531). When the thresholds were combined with all other variables, the 11 cm (0.688) achieved the highest discrimination. CONCLUSION: The discriminant properties of all examined thresholds showed very similar discriminant properties, which brings into questioning whether a dichotomization of pT2 tumours is really necessary.
Purpose. To determine if high-risk prostate cancer responds differently to hypofractionation. Material and methods. One hundred and fifty-seven men with NCCN high-risk (T3, PSA > 20, or Gleason >/= 8) clinically localized prostate cancer treated between 1998 and 2010 met the inclusion criteria for the analysis. Eighty-two were treated with conventional WPRT with a conventionally fractionated sequential boost to the prostate (cRT), with the prostate receiving 75-77 Gy in 1.8-2.0 Gy fractions. Seventy-five were treated with pelvic IMRT with a hypofractionated simultaneous boost to the prostate (hRT), with the prostate receiving 70 Gy in 2.5 Gy fractions. The dose to the pelvic lymph nodes was 45 Gy in the cRT group and 50.4 Gy in the hRT group, both at 1.8 Gy per fraction. Ninety-two percent received neoadjuvant hormonal ablation therapy, typically beginning two months prior to the start of RT. Results. Median follow-up was 6.5 years for men receiving cRT and 3.7 years for those receiving hRT. The actuarial rate of biochemical control at four years was 88% for cRT and 94% for hRT (p = 0.82). The rates of early rectal and urinary grade >/= 2 toxicities were 35% (29 of 82) and 49% (40 of 82) for the cRT group and 36% (27 of 75) and 44% (33 of 75) for the hRT group. The actuarial rate of late grade >/= 2 rectal toxicity at four years was 25% for the cRT group and 13% for the hRT group (p = 0.037). The rate of late grade 3 rectal complications was 4% (3 of 82) for patients receiving cRT and 1% (1 of 75) for patients receiving hRT. Conclusion. Initial follow-up indicates equivalent biochemical control between regimens. Patients receiving hRT experienced fewer late rectal complications.
Materials and Methods: Institutional review board approval was obtained for this retrospective study. Informed consent was waived. From 2007 to 2011, 178 patients with increased PSA levels (mean, 10.7 ng/mL [10.7 mug/L]), previous negative findings of random biopsies, and targets depicted at multiparametric MR imaging underwent transrectal US-guided prostate biopsies after injection of sulfur hexafluoride microbubbles. CE US-targeted biopsies were performed systematically in cancer-suggestive regions, followed by random acquisition of 12 nontargeted cores in all other regions. Diagnostic accuracy of CE US-targeted biopsies was measured with sensitivity, specificity, and positive and negative predictive values. Fisher exact and Mann-Whitney U tests were used to compare subgroups of patients. Potential predictive variables were examined with a logistic regression model. Results: CE US findings were positive in a first group of 158 patients and negative in a second group of 20 patients. Prostate carcinoma (PCa) was detected in 75 patients in the first group (47.5%) and in eight of the second group (40.0%). Overall cancer detection rate was 46.6% (83 of 178). In the first group, PCa was detected with targeted biopsies alone in 18 patients (24%), with nontargeted biopsies alone in 23 (30.7%), and with both in 34 (45.3%). Mean number of CE US-targeted cores per cancer-suggestive region was 2.2. CE US-targeted biopsies had a positive overall detection rate of 30.9%, while it was 6.9% for 12-core nontargeted biopsies (P < .001). PSA level and Gleason score were associated with positivity of CE US-targeted biopsies (P = .031 and P = .015, respectively). Conclusion: Real-time CE US-targeted transrectal US biopsy offers excellent sensitivity for PCa detection in men with previous negative biopsy results and positive findings at multiparametric MR imaging. It may be combined with conventional random biopsies to increase specificity. © RSNA, 2013.
An elevated tumor tissue androgen level, which reactivates androgen receptor in recurrent prostate cancer, arises from the intratumor synthesis of 5alpha-dihydrotestosterone through use of the precursor steroid dehydroepiandrosterone (DHEA) and is fueled by the steroidogenic enzymes 3beta-hydroxysteroid dehydrogenase (3beta-HSD1), aldoketoreductase (AKR1C3), and steroid 5-alpha reductase, type 1 (SRD5A1) present in cancer tissue. Sulfotransferase 2B1b (SULT2B1b) (in short, SULT2B) is a prostate-expressed hydroxysteroid SULT that converts cholesterol, oxysterols, and DHEA to 3beta-sulfates. DHEA metabolism involving sulfonation by SULT2B can potentially interfere with intraprostate androgen synthesis due to reduction of free DHEA pool and, thus, conversion of DHEA to androstenedione. Here we report that in prostatectomy specimens from treatment-naive patients, SULT2B expression is markedly reduced in malignant tissue (P < .001, Mann-Whitney U test) compared with robust expression in adjacent nonmalignant glands. SULT2B was detected in formalin-fixed specimens by immunohistochemistry on individual sections and tissue array. Immunoblotting of protein lysates of frozen cancer and matched benign tissue confirmed immunohistochemistry results. An in-house-developed rabbit polyclonal antibody against full-length human SULT2B was validated for specificity and used in the analyses. Ligand-activated vitamin D receptor induced the SULT2B1 promoter in vivo in mouse prostate and increased SULT2B mRNA and protein levels in vitro in prostate cancer cells. A vitamin D receptor/retinoid X receptor-alpha-bound DNA element (with a DR7 motif) mediated induction of the transfected SULT2B1 promoter in calcitriol-treated cells. SULT2B knockdown caused an increased proliferation rate of prostate cancer cells upon stimulation by DHEA. These results suggest that the tumor tissue SULT2B level may partly control prostate cancer growth, and its induction in a therapeutic setting may inhibit disease progression.

[220]

TÍTULO / TITLE: - Parathyroid hormone-related protein and regulation of cell survival in the kidney.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Kramann R; Schneider RK
INSTITUCIÓN / INSTITUTION: - 1] Department of Nephrology and Clinical Immunology, University Hospital RWTH Aachen, Aachen, Germany [2] Renal Division, Department of Medicine, Brigham and Women’s Hospital, Boston, Massachusetts, USA.
**RESUMEN / SUMMARY:** Parathyroid hormone-related protein (PTHrP) is a pleiotropic factor with multiple physiological functions in morphogenesis, cell proliferation, differentiation, apoptosis, and calcium homeostasis. In the kidney, PTHrP is known to be expressed abundantly and to be upregulated in various experimental nephropathies, showing growth-modulatory and proinflammatory properties. Ardura et al. demonstrate a possible link between PTHrP-induced Runx2 expression and an antiapoptotic effect in tubular epithelial cells.

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**TÍTULO / TITLE:** Hypoxia of PC-3 prostate cancer cells enhances migration and vasculogenesis in vitro of bone marrow-derived endothelial progenitor cells by secretion of cytokines.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Huang S; Peng L; Tang Y; Zhang L; Guo W; Zou X; Peng X

**INSTITUCIÓN / INSTITUTION:** Department of Orthopaedic Surgery/Orthopaedic Research Institute, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong 510080, PR China.

**RESUMEN / SUMMARY:** Hypoxia is a key inducer of neovascularization which is essential for tumor growth, invasion and metastasis. It has been proposed that the recruitment of bone-marrow-derived endothelial progenitor cells (BM-EPCs) is pivotal and requires the participation of several tumor-derived cytokines. However, it is not known whether prostate cancer (PCa) cells contribute to the recruitment and vasculogenesis of EPCs in PCa progression. In the present study, we demonstrated that all conditioned medium (CM) of PC-3 PCa cells promoted proliferation and migration, and augmented the vasculogenesis capacity of BM-EPCs, and 24-h hypoxia (24H)-CM presented stronger ability compared to 24-h normoxia (24N)-CM and 48H-CM. Human cytokine antibody array with 174 anti-cytokine antibodies revealed the changes of cytokine in CMs. Twenty-five types of cytokines significantly increased in 24H-CM compared with 24N-CM. Eleven types of cytokines (5 factors increased and 6 decreased) were significantly different between 48H-CM and 48N-CM. Twelve types of cytokines (4 factors increased and 8 decreased) were significantly different between 48H-CM and 24H-CM. Furthermore, according to the gene ontology analysis, all altered cytokines were involved in proliferation, chemotaxis, cell motility, cell migration, vasculogenesis and angiogenesis. Of note, the changed regularity of cytokines in the 24H-CM and 48H-CM of PC-3 cells was in concert with the functional changes of BM-EPCs treated by different CM of PC-3 cells in enhancing the proliferation, migration and
vasculogenesis potential of BM-EPCs. These findings suggest that PCa cells may have the potential to modulate their microenvironment and facilitate BM-EPC migration and vasculogenesis by secretion of cytokines in the early stage of hypoxia.

[222] TÍTULO / TITLE: - High-resolution ERG-expression profiling on GeneChip exon 1.0 ST arrays in primary and castration-resistant prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Smit FP; Salagierski M; Jannink S; Schalken JA
RESUMEN / SUMMARY: - OBJECTIVE: To assess whether oestrogen-regulated gene (ERG) expression analysis using GeneChip arrays can predict transmembrane protease, serine 2 (TMPRSS2)-ERG fusion. The expression level of the TMPRSS2-ERG gene was studied in various histological grades of prostate cancer and castration-resistant prostate cancer (CPRC). PATIENTS AND METHODS: GeneChip Affymetrix exon 1.0 ST arrays were used for expression profiling of ERG, erythroblast transformation-specific (ETS) variant gene 1 (ETV1), ETV4 and ETV5 genes in 67 prostate cancer tissue specimens. Real-time quantitative polymerase chain reaction analysis and in some cases DNA sequencing was used to validate the presence and the expression levels of TMPRSS2-ERG gene fusions. RESULTS: In our series of patients with prostate cancer over expression of the ERG gene predicted the presence of TMPRSS2-ERG rearrangements in almost all cases. ETS expression by itself outmatched the diagnostic performance of the ERG exons ratioing allowing equal detection of the less frequent ETS gene fusion transcripts. The gene fusions were expressed at significantly lower levels in CPRC but occurred more frequently than in primary prostate cancer. CONCLUSIONS: ERG expression analysis using GeneChip arrays appears to be an excellent diagnostic tool for identifying gene rearrangements. In coming years, measuring expression of the ETS gene family by itself might become a clinically relevant surrogate test to identify patients with fusion-positive prostate cancer. The variation of gene fusion expression levels, particularly in CPRC, needs to be taken into account when using quantitative molecular diagnosis of prostate cancer.
Lesiones liticas en un paciente con antecedentes de cancer renal.

**TÍTULO / TITLE:** - Lytic lesions in a patient with past history of renal cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Sebio A; Robert L; Ovejero D; Murata P; Sullivan I; Stradella A; Maroto P

**INSTITUCIÓN / INSTITUTION:** - Urology Department. Sant Pau Hospital. Barcelona. España.

**RESUMEN / SUMMARY:** - OBJECTIVE: To study lytic lesions in a patient with past history of renal cancer. METHODS: A 62 year-old man was admitted to hospital for investigation of the cause of polyostotic bone pain. RESULTS: Brown tumors due to hyperparathyroidism turned out to be the cause of bone pain. CONCLUSIONS: Differential diagnosis is important in daily practice in order to provide a correct treatment for each condition.

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[224]


**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Taneja SS

**INSTITUCIÓN / INSTITUTION:** - Division of Urologic Oncology, Smilow Comprehensive Prostate Cancer Center, Department of Urology, NYU Langone Medical Center, New York, NY 10016, USA. samir.taneja@nyumc.org

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[225]

**TÍTULO / TITLE:** - ACP Journal Club: review: Serenoa repens does not improve symptom scale scores in benign prostatic hyperplasia.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Mar CD

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[226]
TÍTULO / TITLE: - Stearoyl-CoA Desaturase 1 Is a Novel Molecular Therapeutic Target for Clear Cell Renal Cell Carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - von Roemeling CA; Marlow LA; Wei JJ; Cooper SJ; Caulfield TR; Wu K; Tan WW; Tun HW; Copland JA

INSTITUCIÓN / INSTITUTION: - Authors’ Affiliations: Departments of Cancer Biology, Neuroscience, and Laboratory Medicine and Pathology; and Division of Hematology & Oncology, Mayo Clinic Comprehensive Cancer Center, Jacksonville, Florida.

RESUMEN / SUMMARY: - PURPOSE: We set out to identify Stearoyl-CoA desaturase 1 (SCD1) as a novel molecular target in clear cell renal cell carcinoma (ccRCC) and examine its role in tumor cell growth and viability in vitro and in vivo independently as well as in combination with current U.S. Food and Drug Administration (FDA)-approved regimens. EXPERIMENTAL DESIGN: Patient normal and ccRCC tissue samples and cell lines were examined for SCD1 expression. Genetic knockdown models and targeted inhibition of SCD1 through use of a small molecule inhibitor, A939572, were analyzed for growth, apoptosis, and alterations in gene expression using gene array analysis. Therapeutic models of synergy were evaluated utilizing pharmacologic inhibition of SCD1 with the tyrosine kinase inhibitors (TKI) sunitinib and pazopanib, and the mTOR inhibitor temsirolimus. RESULTS: Our studies identify increased SCD1 expression in all stages of ccRCC. Both genetic knockdown and pharmacologic inhibition of SCD1 decreased tumor cell proliferation and induced apoptosis in vitro and in vivo. Upon gene array, quantitative real-time PCR, and protein analysis of A939572-treated or SCD1 lentiviral knockdown samples, induction of endoplasmic reticulum stress response signaling was observed, providing mechanistic insight for SCD1 activity in ccRCC. Furthermore, combinatorial application of A939572 with temsirolimus synergistically inhibited tumor growth in vitro and in vivo. CONCLUSIONS: Increased SCD1 expression supports ccRCC viability and therefore we propose it as a novel molecular target for therapy either independently or in combination with an mTOR inhibitor for patients whose disease cannot be remedied with surgical intervention, such as in cases of advanced or metastatic disease. Clin Cancer Res; 19(9); 2368-80. ©2013 AACR.

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[227]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hsieh CI; Lung AL; Chang LI; Sampselle CM; Lin CC; Liao YM

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan; Division of Hematology and Oncology, Department of Internal Medicine, Taipei Medical University Hospital, Taipei, Taiwan.

RESUMEN / SUMMARY: - BACKGROUND: Few studies conducted outside of Asia have shown that lower urinary tract symptoms (LUTS) could be a concern for cancer patients. This gap necessitates more research on LUTS among cancer patients in Asia, particularly regarding associated factors and the relationship between quality of life and LUTS. OBJECTIVES: This study investigates the prevalence, associated factors, and relationship to quality of life of LUTS based on a sample of cancer patients. DESIGN: A cross-sectional, questionnaire survey. SETTINGS/PARTICIPANTS: This study was conducted at two oncology outpatient departments in two hospitals in Taiwan, and included 134 Asian cancer patients. METHODS: We collected information about each participant’s individual characteristics, personal habits, LUTS, and quality of life by using a questionnaire. We calculated descriptive statistics to demonstrate the distribution of collected information, and used multivariate logistic regression to identify the factors associated with LUTS. We used Student’s t-test to compare the mean quality of life scores for participants with and without LUTS. RESULTS: Ninety-nine (73.9%) participants experienced at least one type of LUTS, and the prevalence rates for various types of LUTS ranged from 3.7% to 52.2%. Radiotherapy and the time since the diagnosis of cancer were associated with LUTS. Participants with LUTS reported lower quality of life scores than participants without LUTS. CONCLUSIONS: The high prevalence of LUTS suggests that cancer treatment might be linked to LUTS, which in turn has a negative effect on a patient’s quality of life. These results suggest that future research should involve studies in larger, more homogeneous samples. Health care providers should monitor the presence of LUTS and deliver the management and treatments of LUTS to optimise cancer patients’ quality of life.

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[228]
**TÍTULO / TITLE:** - Re: significance of docetaxel-based chemotherapy as treatment for metastatic castration-resistant prostate cancer in Japanese men over 75 years old.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](10.1016/j.juro.2012.12.047)


**AUTORES / AUTHORS:** - Griebling TL

[229]

**TÍTULO / TITLE:** - Delayed radiotherapy for patients with localized prostate cancer: validation by propensity score matching.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](Anticancer Res. 2013 Apr;33(4):1629-33)


**AUTORES / AUTHORS:** - Nakayama H; Kanemoto A; Kikuchi K; Matsuki K; Tomobe M; Tsukamoto S; Takeshima H; Oshiro Y; Sugahara S; Tokuuye K

**INSTITUCIÓN / INSTITUTION:** - Department of Radiation Oncology, Tsukuba Medical Center, Tsukuba, Ibaraki, Japan. [hnakayam@tokyo-med.ac.jp](mailto:hnakayam@tokyo-med.ac.jp)

**RESUMEN / SUMMARY:** - AIM: To retrospectively investigate the biochemical outcome following delayed radiotherapy in patients with prostate cancer.

PATIENTS AND METHODS: From July 2000 to November 2008, 144 consecutive patients with localized prostate cancer underwent radiotherapy and androgen-deprivation therapy. Biochemical progression-free survival was compared in patients who began radiotherapy >6 months (delayed group) with those who began <= 6 months (non-delayed group) from diagnosis by biopsy. Treatment selection bias was adjusted by the propensity score method.

RESULTS: After a median follow-up of 64 months, the 5-year biochemical progression-free survival of the delayed and non-delayed groups was 87.4% (95% confidence interval, CI=69.7-95.1%) and 96.6% (95% CI=89.6-98.9%), respectively (p=0.03). Delayed radiotherapy was the only independent risk factor for biochemical progression (hazard ratio=3.97, 95% CI 1.07-14.7, p=0.04). The results were validated by propensity score analysis.

CONCLUSION: Delaying radiotherapy by >6 months increases the risk of biochemical progression in patients with localized prostate cancer.

[230]

**TÍTULO / TITLE:** - Polyunsaturated Fatty Acids Affect the Localization and Signaling of PIP3/AKT in Prostate Cancer Cells.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](1093/carcin/bgt147)

**REVISTA / JOURNAL:** - Carcinogenesis. 2013 Apr 30.
AKT is a serine-threonine protein kinase that plays important roles in cell growth, proliferation and apoptosis. It is activated after binding to phosphatidylinositol phosphates (PIPs) with phosphate groups at positions 3, 4 and 3,4,5 on the inositol ring. In spite of extensive research on AKT, one aspect has been largely overlooked, namely the role of the fatty acid chains on PIPs. PIPs are phospholipids composed of a glycerol backbone with fatty acids at the sn-1 and sn-2 position and inositol at the sn-3 position. Here we show that polyunsaturated fatty acids (PUFA) modify phospholipid content. Docosahexaenoic acid (DHA), an omega3 PUFA, can replace the fatty acid at the sn-2 position of the glycerol backbone, thereby changing the species of phospholipids. DHA also inhibits AKT-T308 but not AKT-S473 phosphorylation, alters PI(3,4,5)P3 (PIP3) and phospho-AKT-S473 protein localization, decreases pPDPK1-S241-AKT and AKT-BAD interaction, and suppresses prostate tumor growth. Our study highlights a potential novel mechanism of cancer inhibition by omega3 PUFA through alteration of PIP3 and AKT localization and affecting the AKT signaling pathway.

[231]

Fluid intake, genetic variants of UDP-glucuronosyltransferases, and bladder cancer risk.

Background: Results of studies of fluid consumption and its association with bladder cancer have been inconsistent. Few studies have considered modification effects from genetic variants that may interact with the type of consumed fluids. UDP-glucuronosyltransferases (UGTs), which are membrane-bound conjugating enzymes, catalyse the transformation of hydrophobic substrates to more water-soluble glucuronides to facilitate renal or biliary excretion. Whether genetic variants in UGTs could modulate the association between fluid intake and bladder cancer has not been studied. Methods: We conducted a case-control study with 1007 patients with
histopathologically confirmed bladder cancer and 1299 healthy matched controls. Fluid intake and epidemiologic data were collected via in-person interview. Multivariate unconditional logistic regression was used to estimate odds ratios (ORs) and the 95% confidence intervals (95% CI). Results: After adjustment for potential confounders, high quantity of total fluid intake (≥2789 vs <1696 ml per day) conferred a 41% increased risk of bladder cancer (OR=1.41; 95% CI=1.10-1.81). Specific fluids such as regular soft drinks and decaffeinated coffee were also associated with increased risks, whereas tea, wine, and liquor were associated with decreased risks. Among 83 single-nucleotide polymorphisms in the UGT gene family, 18 were significantly associated with bladder cancer risk. The most significant one was rs7571337, with the variant genotype conferring a 29% reduction in risk (OR=0.71; 95% CI=0.56-0.90). Conclusions: Total and specific fluid intakes are associated with bladder cancer risk in the study population and that genetic variants of UGT genes could modulate the effects. These results facilitate identification of high-risk individuals and have important implications in bladder cancer prevention. British Journal of Cancer advance online publication, 30 April 2013; doi:10.1038/bjc.2013.190 www.bjcancer.com.
impact of pre-treatment clinical factors [T stage, PSA, and Gleason score (GS)].

RESULTS: At a median follow-up time of 62 months, actuarial bDFS, DMFS, CSS, and OS at 5 years were 64.8, 85.2, 95.8, and 94.4 %, respectively. On multivariate analysis, only GS was significantly associated with three clinical endpoints (bDFS: HR 1.6; p = 0.022, CSS: HR 4.27, p = 0.044, OS: HR 2.6; p = 0.038). Pre-treatment zenith PSA was associated only with bDFS (HR 1.87; p = 0.027).

CONCLUSIONS: Patients with “high” PSA levels (>/=20 ng/mL) showed favorable clinical outcomes, supporting the role of local radiotherapy as primary therapy in combination with long-term ADT in patients with high PSA levels at diagnosis. A GS of 8-10 is the strongest predictor of outcome.

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[233] TÍTULO / TITLE: - Does age really matter in the choice of treatment for bladder cancer?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.239
AUTORES / AUTHORS: - Moro FD; Rossi A; Zattoni F
INSTITUCIÓN / INSTITUTION: - Department of Surgical, Oncological and Gastroenterological Sciences-Urology, University of Padova, Via Giustiniani 2, 35126 Padova, Italy.

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RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Zhang N; Ye L; Wu L; Deng X; Yang Y; Jiang WG
INSTITUCIÓN / INSTITUTION: - Department of Urology, Beijing Chaoyang Hospital, Capital Medical University No. 8, Gongti South Road, Chaoyang District, Beijing 100020, P.R. China, E-mail: niru7429@yahoo.com.cn or Professor Wen G. Jiang, Cardiff University School of Medicine, Heath Park, Cardiff CF14 4XN, U.K. jiangw@cf.ac.uk.
RESUMEN / SUMMARY: - BACKGROUND: Bone morphogenetic protein-10 (BMP10), a novel member of the bone morphogenetic protein (BMP) family, has been indicated as a possible tumour suppressor in prostate and breast cancer. However, its role in urothelial tumours remains unknown. In the present study, we examined the role of BMP10 in urothelial cancer cells and the expression of BMP10 in human urothelial cancer of the bladder. MATERIALS AND METHODS: The expression of BMP10 was examined in human bladder tissues
and in the T24 human bladder cancer cell line using immunochemical staining and reverse transcription polymerase chain reaction (RT-PCR), respectively. The biological impact of modifying BMP10 expression, through genetic manipulation, in urothelial cancer cells was evaluated using in vitro models.

RESULTS: mRNA for BMP10 and receptors of BMPs was expressed in T24 cell lines. BMP10 protein expression was observed in normal urothelial and stromal cells, but was found to be decreased in or absent from urothelial cancer cells. The frequency of positive staining in normal tissues (9/9) was significantly higher than that in urothelial cancer tissues (6/15) (p=0.007). T24 cells were transfected with BMP10 expression plasmid. It was further demonstrated that overexpression of BMP10 reduced the growth rate of T24 cells, and markedly reduced the motility, and adhesion of T24 cells in vitro. No significant effects were seen on in vitro invasiveness of T24 cells following BMP10 transfection.

CONCLUSION: Expression of BMP10 protein is reduced in cancer cells of bladder tumours. Overexpression of BMP10 has an inhibitory effect on the growth, adhesion, and migration of bladder cancer cells in vitro. This would suggest a potential tumour suppressor role of BMP10 in bladder cancer.
INSTITUCIÓN / INSTITUTION: - Department of Urology, West China Hospital, Sichuan University, Chengdu, Sichuan, People’s Republic of China.

RESUMEN / SUMMARY: - OBJECTIVE: To analyze the clinical characteristics, treatment modalities, and outcomes of adult prostate sarcoma treated at our institution. MATERIALS AND METHODS: The medical records of 25 adult patients with prostate sarcoma were obtained from January 1989 to December 2009. The clinicopathologic parameters were evaluated to determine their effect on survival. RESULTS: The median age was 37 years (range 18-81). The median tumor size was 9.5 cm (range 4-25). The median serum prostate-specific antigen level was 1.39 ng/mL (range 0.39-33.20). The most common symptom was dysuria (72%). Transrectal ultrasound-guided needle biopsy was used to diagnose 22 sarcomas, transurethral resection of the prostate to diagnose 2, and open surgery to diagnose 1. The predominant histologic subtype was leiomyosarcoma (40%); 21 (88%) were high grade and 6 patients had metastatic disease. Surgical resection of curative intent was performed in 14 patients, with negative margins in 10. After a median follow-up of 21 months (range 5-63), 2 patients were disease free, 4 were alive with disease, and 19 had died of their disease. Overall, the 1-, 2-, 3-, and 5-year survival rate was 80.0%, 47.4%, 22.6%, and 11.3%, respectively, and the median survival time was 23 months. The median survival time after recurrence was 20 months (range 9-39) and that after metastasis was 10 months (range 3-23). Age >50 years, metastasis at presentation, and a lack of surgery with curative intent were independently predictive of an unfavorable outcome. CONCLUSION: Adult prostate sarcoma accounted for 0.7% of primary prostate malignancies and carried a poor prognosis. Early diagnosis and surgical resection with curative intent offer patients the best chance of survival.

[237]

TÍTULO / TITLE: - Protein tyrosine phosphatase zeta enhances proliferation by increasing beta-catenin nuclear expression in VHL-inactive human renal cell carcinoma cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Shang D; Xu X; Wang D; Li Y; Liu Y

INSTITUCIÓN / INSTITUTION: - Department of Urology, Beijing Friendship Hospital, Capital Medical University, Beijing, 100050, China.

RESUMEN / SUMMARY: - OBJECTIVE: We investigated the role of protein tyrosine phosphatase zeta (Ptprz1) in human renal cell carcinoma (RCC) cells’ proliferation and associations between Ptprz1 expression and von Hippel-Lindau (VHL) activation. METHODS: A normal human renal cell line and four
human RCC cell lines were used in this study. VHL or Ptprz1 expression in RCC cells was increased by transfection with a VHL or Ptprz1 vector. VHL or Ptprz1 expression was decreased in these cells by siRNA using Lipofectamine 2000. Cells' proliferative activity was assessed by WST-1 assay. RESULTS: Our results suggested that Ptprz1 was a target of VHL, and a loss of VHL activation increased Ptprz1 expression in RCC cells. Ptprz1 enhanced beta-catenin protein expressions in the nuclear fractions of RCC cells and participated in regulating proliferation by activating beta-catenin and its downstream genes. In addition, a loss of VHL activity may enhance the proliferative activity of RCC cells by increasing Ptprz1 expression.

CONCLUSION: Ptprz1-enhanced RCC cells' proliferation depends on VHL inactivation, and the Ptprz1/beta-catenin pathway may be a potential target for treating RCC with inactive VHL.

[238]
**TÍTULO / TITLE:** Re: 20-Year Survival After Radical Prostatectomy as Initial Treatment for cT3 Prostate Cancer.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**AUTORES / AUTHORS:** Taneja SS

[239]
**TÍTULO / TITLE:** Re: comparison of oncological outcomes after segmental ureterectomy or radical nephroureterectomy in urothelial carcinomas of the upper urinary tract: results from a large French multicentre study.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**AUTORES / AUTHORS:** Laguna MP

[240]
**TÍTULO / TITLE:** The effect of antibiotherapy on PSA levels and prostate biopsy results in patients with PSA levels 2.5-10 ng/mL.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
**REVISTA / JOURNAL:** J Endourol. 2013 May 5. ●●Enlace al texto completo (gratuito o de pago) 1089/end.2013.0022
Aim: This controlled prospective study aims to investigate the possible effects of antibiotic treatment on prostate specific antigen (PSA) and its derivatives, and consequently on the transrectal biopsy rates, in the diagnosis of prostate cancer. Patients and Methods: 140 patients between 45 and 70 years old, with a PSA level between 2.5 and 10 ng/ml and normal digital rectal examinations (DRE), were included in this study between June 2009 and November 2010. The patients were randomly assigned into two groups. The first group received levofloxacin 500 mg (p.o.) 1*1 for 21 days; the second, the control group, was given no treatment. Initially, total PSA (tPSA), free PSA (fPSA), a DRE, urinary ultrasonography (including prostate volume, post voiding residual urine), uroflowmetry, International Prostate Symptom Score (IPSS), National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) and International Index of Erectile Function (IIEF) tests were performed. All of these were repeated at the end of three weeks of antibiotic treatment. An additional PSA measurement was also done at 10th day of the treatment. All patients underwent transrectal ultrasonography (TRUS) guided prostate biopsy at 21st day. Results: The mean age of the patients was 59.6. Overall in 23 patients, prostate cancer was detected. Statistically, there were significant changes in values of PSA and its derivatives in the treatment group (from 5.31 to 4.69 and 4.58 ng/ml). However, focusing on prostate cancer patients in both, the treatment and control, groups; we did not detect any significant change in the same parameters. Conclusion: Antibiotic treatment given to the patients with a PSA level between 2.5 and 10 ng/ml can be beneficial, prior to a decision for TRUS guided prostate biopsy, just in a limited subgroup. However, considering the large population of patients in the gray zone, it still does not provide clear solid evidence for avoiding unnecessary prostate biopsies.
BORIS and CTCF are paralogous, multivalent 11-zinc finger transcription factors that play important roles in organizing higher-order chromatin architecture. BORIS is a cancer-testis antigen with a poorly defined function in cancer, although it has been hypothesized to exhibit oncogenic properties. CTCF, however, has been postulated as a candidate tumor suppressor. We collated the genetic lesions in BORIS and CTCF from multiple cancers identified using high-throughput genomics. In BORIS, nonsense and missense mutations are evenly distributed. In CTCF, recurrent mutations are mostly clustered in the conserved zinc finger domain and at residues critical for contacting DNA and zinc ion co-ordination. Three missense mutations are common to both proteins. We used an inducible lentivector to express wildtype BORIS or CTCF in primary cells and cancer cell lines in order to define their functional differences. Both BORIS and CTCF caused a significant decrease in cell proliferation and clonogenic capacity, without alteration of specific cell cycle phases. Both BORIS and CTCF conferred protective effects in primary cells and some cancer cells during UV damage-induced apoptosis. Using a bioluminescent MCF-7 orthotopic breast cancer model in vivo, we demonstrated that CTCF and BORIS suppressed breast cancer growth. These findings provide further evidence that CTCF behaves as a tumor suppressor, and show BORIS has a similar growth inhibitory effect in vitro and in vivo. Hence, acquired zinc finger mutations may disrupt these functions, thereby contributing to tumor growth and development.

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chromosome 8q24 locus play important roles in cancer development in general.

STUDY DESIGN, SIZE, DURATION: We have conducted a population-based Norwegian-Swedish case-parent study, based on cases diagnosed in 1990-2008, including 831 triads (TGCT case and both parents), 474 dyads (TGCT case and one parent) and 712 singletons (only the TGCT case). In addition we expanded the study to include 3922 unrelated male controls from the TwinGene project.

PARTICIPANTS/MATERIALS, SETTING, METHODS: We genotyped 26 single nucleotide polymorphisms (SNPs) in AKT1, PTEN and the 8q24 locus. First, triads and dyads were included in a likelihood-based association test. To increase the statistical power, case singletons and controls from the TwinGene project were included in a single test for association. We examined if the allelic effect on TGCT risk differed by histological subgroup, country of origin or parent of origin. Odds ratios (ORs) and 95% confidence intervals (CI) were calculated with Bonferroni correction (Pbonf) for multiple testing. MAIN RESULTS AND THE ROLE OF CHANCE: In the case-parent analyses, none of the 26 SNPs were significantly associated with TGCT. Of the 23 SNPs investigated in the combined study, one SNP in PTEN (rs11202586) remained associated with TGCT risk after adjusting for multiple testing (OR = 1.16, 95% CI = 1.06-1.28, Pbonf = 0.040). We found no difference in risk according to histological subgroup, parent of origin or between countries. LIMITATIONS, REASONS FOR CAUTION: Our study is strengthened by the population-based design and large sample size, which gives high power to detect risk alleles. The reported association was not highly significant, and although it was based on an a priori hypothesis of this tumor suppressor gene being implicated in the etiology of TGCT, replication studies, as well as functional studies of this polymorphism, are warranted. WIDER IMPLICATIONS OF THE FINDINGS: We report, to our knowledge, a novel association between TGCT and a marker in the tumor suppressor gene PTEN. Previous studies have linked PTEN to TGCT etiology, and there is also a link between PTEN and KITLG, which contains TGCT susceptibility loci revealed through recent genome-wide studies.

STUDY FUNDING/COMPETING INTEREST(S): This work was financially supported by the Norwegian Cancer Society (418975) and the Nordic Cancer Union (S-12/07). No competing interests are declared.

[243]

TÍTULO / TITLE: Tobacco use and external beam radiation therapy for prostate cancer: Influence on biochemical control and late toxicity.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1002/oncrr.28128

AUTORES / AUTHORS: Solanki AA; Liauw SL
INSTITUCIÓN / INSTITUTION: - Department of Radiation and Cellular Oncology, University of Chicago Medical Center, Chicago, Illinois.

RESUMEN / SUMMARY: - BACKGROUND: The objective of this study was to examine the effect of tobacco use on disease control and late gastrointestinal and genitourinary toxicity in men undergoing external beam radiotherapy (EBRT) for prostate cancer. METHODS: In total, 633 men with known tobacco history at consultation underwent definitive EBRT between 1988 and 2008. Tobacco use was defined as positive (current or prior) or negative (never). The median EBRT dose was 74 gray (Gy). In univariate analysis, tobacco use and other prognostic factors were compared with disease control and toxicity. Multivariable analysis included tobacco use and the covariates that were associated with outcome on univariate analysis (P < .1). RESULTS: The rate of 5-year freedom from biochemical failure (FFBF) was 76% for current smokers, 81% for prior smokers, and 87% for never smokers (P < .02). Risk group, the percentage of involved cores, and EBRT dose >/= 74 Gy were associated with FFBF (all P < .01). On multivariable analysis, smoking was not associated with FFBF (P = .19). Factors that were associated with late grade >/= 2 genitourinary toxicity on univariate analysis included positive tobacco history, intensity-modulated radiotherapy, and EBRT dose >/= 74 Gy (all P < .05). Prior transurethral resection of the prostate (P < .01) and current smoking status (P = .06) were associated with grade >/= 3 toxicity. On multivariable analysis, a positive tobacco history was associated with grade >/= 2 toxicity (hazard ratio, 1.45; P < .02), and current smoking status was associated with grade >/= 3 toxicity (hazard ratio, 3.02; P < .05). Tobacco use was not associated with late gastrointestinal toxicity. CONCLUSIONS: In men who are receiving EBRT for prostate cancer, tobacco use may be associated with higher rates of late grade >/= 2 toxicity, and current smokers may have higher rates of late grade >/= 3 genitourinary toxicity. Cancer 2013. © 2013 American Cancer Society.

[244]

TÍTULO / TITLE: - Role of androgen and vitamin D receptors in endothelial cells from benign and malignant human prostate.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Godoy AS; Chung I; Montecinos VP; Buttyan R; Johnson CS; Smith GJ

INSTITUCIÓN / INSTITUTION: - Dept. of Physiology, Pontificia Universidad Catolica de Chile, Alameda 340, Santiago de Chile. agodoy@bio.puc.cl.
Forty years ago, Judah Folkman (Folkman. N Engl J Med 285: 1182-1186, 1971) proposed that tumor growth might be controlled by limiting formation of new blood vessels (angiogenesis) needed to supply a growing tumor with oxygen and nutrients. To this end, numerous “antiangiogenic” agents have been developed and tested for therapeutic efficacy in cancer patients, including prostate cancer (CaP) patients, with limited success. Despite the lack of clinical efficacy of lead anti-angiogenic therapeutics in CaP patients, recent published evidence continues to support the idea that prostate tumor vasculature provides a reasonable target for development of new therapeutics. Particularly relevant to antiangiogenic therapies targeted to the prostate is the observation that specific hormones can affect the survival and vascular function of prostate endothelial cells within normal and malignant prostate tissues. Here, we review the evidence demonstrating that both androgen(s) and vitamin D significantly impact the growth and survival of endothelial cells residing within prostate cancer and that systemic changes in circulating androgen or vitamin D drastically affect blood flow and vascularity of prostate tissue. Furthermore, recent evidence will be discussed about the expression of the receptors for both androgen and vitamin D in prostate endothelial cells that argues for direct effects of these hormone-activated receptors on the biology of endothelial cells. Based on this literature, we propose that prostate tumor vasculature represents an unexplored target for modulation of tumor growth. A better understanding of androgen and vitamin D effects on prostate endothelial cells will support development of more effective angiogenesis-targeting therapeutics for CaP patients.
logistic regression. Positive predictive values for features of kidney cancer were estimated. RESULTS: Cases consulted more frequently than controls in the year before diagnosis: median 16 consultations (interquartile range 10-25) versus 8 (4-15); P<0.001. Fifteen features were independently associated with kidney cancer: visible haematuria, odds ratio 37 (95% confidence interval [CI] = 28 to 49), abdominal pain 2.8 (95% CI = 2.4 to 3.4), microcytosis 2.6 (95% CI = 1.9 to 3.4), raised inflammatory markers 2.4 (95% CI = 2.1 to 2.8), thrombocytosis 2.2 (95% CI = 1.7 to 2.7), low haemoglobin 1.9 (95% CI = 1.6 to 2.2), urinary tract infection 1.8 (95% CI = 1.5 to 2.1), nausea 1.8 (95% CI = 1.4 to 2.3), raised creatinine 1.7 (95% CI = 1.5 to 2.0), leukocytosis 1.5 (95% CI = 1.2 to 1.9), fatigue 1.5 (95% CI = 1.2 to 1.9), constipation 1.4 (95% CI = 1.1 to 1.7), back pain 1.4 (95% CI = 1.2 to 1.7), abnormal liver function 1.3 (95% CI = 1.2 to 1.5), and raised blood sugar 1.2 (95% CI = 1.1 to 1.4). The positive predictive value for visible haematuria in patients aged >/=60 years was 1.0% (95% CI = 0.8 to 1.3). CONCLUSION: Visible haematuria is the commonest and most powerful single predictor of kidney cancer, and the risk rises when additional symptoms are present. When considered alongside the risk of bladder cancer, the overall risk of urinary tract cancer from haematuria warrants referral.

[246]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Vanasek J; Odrazka K; Dolezel M; Kolarova I; Jarkovsky J; Pavlik T; Hlavka A; Dusek L
INSTITUCIÓN / INSTITUTION: - Department of Radiation and Clinical Oncology, Multiscan Pardubice, Pardubice, Czech Republic.
RESUMEN / SUMMARY: - PURPOSE: The study aimed to analyze the dose-volume profiles of 3-dimensional radiation therapy (3D-CRT) and intensity modulated RT (IMRT) in the treatment of prostate carcinoma and to specify the profiles responsible for the development of gastrointestinal (GI) toxicity. METHODS AND MATERIALS: In the period 1997 to 2007, 483 patients with prostate carcinoma in stage T1-3 N0 (pN0) M0 were treated with definitive RT. Two groups of patients were defined for the analysis: the 3D-CRT group (n=305 patients) and the IMRT group (n=178 patients). In the entire cohort of 483 patients, the median follow-up time reached 4.4 years (range, 2.0-11.7 years). The cumulative absolute and relative volumes of irradiated rectum exposed to a
given dose (area under the dose-volume curve, AUC) were estimated. The receiver operating characteristic analysis was then used to search for the optimal dose and volume cutoff points with the potential to distinguish patients with enhanced or escalated toxicity. RESULTS: Despite the application of high doses (78-82 Gy) in the IMRT group, GI toxicity was lower in that group than in the group treated by 3D-CRT with prescribed doses of 70 to 74 Gy. Both RT methods showed specific rectal dose-volume distribution curves. The total AUC values for IMRT were significantly lower than those for 3D-CRT. Furthermore, IMRT significantly decreased the rectal volume receiving low to intermediate radiation doses in comparison with 3D-CRT; specific cutoff limits predictable for the level of GI toxicity are presented and defined in our work. CONCLUSIONS: Total area under the dose-volume profiles and specific cutoff points in low and intermediate dose levels have significant predictive potential toward the RT GI toxicity. In treatment planning, it seems that it is valuable to take into consideration the entire dose-volume primary distribution.
There are limited data about bone turnover markers (BTM) in androgen deprivation therapy (ADT)-treated prostate cancer (PCa) patients, and the relationship between sex steroids, bone mass, and BTM has not been explored. Our objective was to analyze the influence of sex steroids levels on BTM in patients with PCa treated with or without ADT. We performed a cross-sectional study including 83 subjects with PCa (54% with ADT). BTM, bone mineral density (BMD), and sex steroids were determined. BTM were inversely related to serum level of estrogens. Tartrate-specific acid phosphatase (TRAP-5b) showed a negative correlation with free estradiol (Free E) \((r = -0.274, p = 0.014)\) and Bio E \((r = -0.256, p = 0.022)\) that remained after adjustment for age: Free E \((\text{beta} = -0.241, p = 0.03)\) and Bio E \((\text{beta} = -0.213, p = 0.063)\). Bone-specific alkaline phosphatase (BSAP) concentrations were inversely related to Free E \((r = -0.281, p = 0.011, \text{age adjusted beta} = -0.256, p = 0.024)\). There was a negative correlation between osteocalcin (OC) levels and Free E \((r = -0.195, p = 0.082; \text{age adjusted beta} = -0.203, p = 0.076)\) and Bio E \((r = -0.215, p = 0.054; \text{age adjusted beta} = -0.240, p = 0.039)\). BTM and androgens were inversely related to TRAP-5b: total testosterone (total T) \((r = -0.238, p = 0.033)\), Free T \((r = -0.309, p = 0.05)\), and Bio T \((r = -0.310, p = 0.05)\), but these correlations disappeared after age-adjustment. We did not find any relationship between BMD at different locations and sex steroids. In conclusion, in patients with PCa, estrogen levels influence bone resorption and bone formation whereas androgens may exert actions only in bone resorption. These results suggest that estradiol is the main sex steroid that regulates bone metabolism in males with prostate carcinoma.

Targeted MRI-guided Prostate Biopsies for the Detection of Prostate Cancer: Initial Clinical Experience With Real-time 3-Dimensional Transrectal Ultrasound Guidance and Magnetic Resonance/Transrectal Ultrasound Image Fusion.

In conclusion, in patients with PCa, estrogen levels influence bone resorption and bone formation whereas androgens may exert actions only in bone resorption. These results suggest that estradiol is the main sex steroid that regulates bone metabolism in males with prostate carcinoma.
OBJECTIVE: To prove the feasibility and evaluate the initial clinical results of targeted prostate biopsies using the Urostation novel platform using magnetic resonance imaging (MRI)/transrectal ultrasound (TRUS) registration to help steer the biopsy needle to suspicious areas.

METHODS: We prospectively included 30 patients for suspicion of prostate cancer from November 2011 to August 2012. All patients were previously evaluated by a multiparametric MRI, interpreted by a single radiologist who attributed a Prostate Imaging-Reporting and Data System (PI-RADS) score to each lesion. A conventional 12-core randomized biopsy protocol was performed and 2 additional targeted biopsies were performed on suspicious area(s). The results of randomized and targeted biopsies were compared.

RESULTS: Among the 30 patients, suspicious area(s) were found on MRI in 20 cases (67%). Median procedure time was 23 minutes. Targeting success rate (biopsy visualized inside the target) was 83%, with at least 1 biopsy reaching the target in all cases. Prostate cancer was detected in 14 cases (47%), including 11 cases with an abnormal MRI. Targeted biopsies detected cancer in all 11 cases and all but 1 were clinically significant. Randomized biopsies detected 10 of these 11 cases, and 3 more cases that MRI considered normal. Sensitivity to detect a significant cancer was 91% in both modalities.

CONCLUSION: This initial clinical study showed encouraging results for targeted MRI-guided prostate biopsies using MRI-TRUS fusion. Although further studies are needed to determine the role of prostate MRI before biopsy and the relevance of targeted biopsies, the Urostation is an MRI-TRUS fusion device that has good accuracy for targeting suspicious areas on MRI.
RESUMEN / SUMMARY: - PURPOSE: To explore the correlation between hepatocyte cell adhesion molecule (hepaCAM) and activated mammalian target of rapamycin (p-mTOR) in transitional cell carcinoma of bladder (TCCB) and whether the anti-proliferation effect of hepaCAM is associated with AMPK/mTOR pathway. MATERIALS AND METHODS: QRT-PCR was used to examine the mRNA expression of hepaCAM and western blot was used to measure the protein level of hepaCAM and p-mTOR in 25 men and 5 women. Disease was Ta-T1 in 7 patients, T2-T4 in 23, G1 in 13, G2 in 9, G3 in 8, primary in 13 and recurrent in 17. WST-8 assay was used to study the effect of hepaCAM on the ability of cellular proliferation. P-AMPK, p-mTOR, total AMPK, total mTOR, c-Myc and cyclin D1 were also determined by western blot. RESULTS: HepaCAM mRNA and protein were significantly decreased, while p-mTOR protein was remarkably increased in TCCB compared to adjacent tissues (P<0.01, P<0.01). The analysis of spearman correlation showed that the decrease of hepaCAM level was associated with the increase of p-mTOR level (r=-0.533 P=0.002). Furthermore, hepaCAM inhibited the proliferation of human TCCB cells. Over-expression of hepaCAM activated AMPK, down-regulated p-mTOR and its targets, c-myc and cyclin D1. Treatment with AMPK inhibitor (Compound C) prevented the anti-proliferation effect of hepaCAM. Compound C completely blocked hepaCAM induced activation of AMPK, down-regulation of p-mTOR and its targets, c-Myc and cyclin D1. CONCLUSIONS: The results suggest an important correlation between hepaCAM and p-mTOR. HepaCAM can inhibit the proliferation of bladder cancer cells through an AMPK/mTOR-dependent pathway.

[252]

TÍTULO / TITLE: - A novel histone deacetylase (HDAC) inhibitor MHY219 induces apoptosis via up-regulation of androgen receptor expression in human prostate cancer cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Patra N; De U; Kim TH; Lee YJ; Ahn MY; Kim ND; Yoon JH; Choi WS; Moon HR; Lee BM; Kim HS

INSTITUCIÓN / INSTITUTION: - Laboratory of Molecular Toxicology, College of Pharmacy, Pusan National University, San 30, Jangjeon-dong, Geumjeung-gu, Busan 609-735, Republic of Korea.

RESUMEN / SUMMARY: - Histone deacetylase (HDAC) inhibitors are a new class of anticancer agents that act by inhibiting cancer cell proliferation and inducing apoptosis in various cancer cell lines. To investigate the anticancer effect of a
novel histone deacetylase (HDAC) inhibitor MHY219, its efficacy was compared to that of suberoylanilide hydroxamic acid (SAHA) in human prostate cancer cells. The anticancer effects of MHY219 on cell viability, HDAC enzyme activity, cell cycle regulation, apoptosis and other biological assays were performed. MHY219 was shown to enhance the cytotoxicity on DU145 cells (IC50, 0.36μM) when compared with LNCaP (IC50, 0.97μM) and PC3 cells (IC50, 5.12μM). MHY219 showed a potent inhibition of total HDAC activity when compared with SAHA. MHY219 increased histone H3 hyperacetylation and reduced the expression of class I HDACs (1, 2 and 3) in prostate cancer cells. MHY219 effectively increased the sub-G1 fraction of cells through p21 and p27 dependent pathways in DU145 cells. MHY219 significantly induced a G2/M phase arrest in DU145 and PC3 cells and arrested the cell cycle at G0/G1 phase in LNCaP cells. Furthermore, MHY219 effectively increased apoptosis in DU145 and LNCaP cells, but not PC3 cells, according to Annexin V/PI staining and Western blot analysis. These results indicate that MHY219 is a potent HDAC inhibitor that targets regulating multiple aspects of cancer cell death and might have preclinical value in human prostate cancer chemotherapy, warranting further investigation.

[253]

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TÍTULO / TITLE: - Putrescine Importer PlaP Contributes to Swarming Motility and Urothelial Cell Invasion in Proteus mirabilis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kurihara S; Sakai Y; Suzuki H; Muth A; Phanstiel O 4th; Rather PN
INSTITUCIÓN / INSTITUTION: - From the Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, Georgia 30322.
RESUMEN / SUMMARY: - Previously, we reported that the speA gene, encoding arginine decarboxylase, is required for swarming in the urinary tract pathogen Proteus mirabilis. In addition, this previous study suggested that putrescine may act as a cell-to-cell signaling molecule (Sturgill, G., and Rather, P. N. (2004) Mol. Microbiol. 51, 437-446). In this new study, PlaP, a putative putrescine importer, was characterized in P. mirabilis. In a wild-type background, a plaP null mutation resulted in a modest swarming defect and slightly decreased levels of intracellular putrescine. In a P. mirabilis speA mutant with greatly reduced levels of intracellular putrescine, plaP was required for the putrescine-dependent rescue of swarming motility. When a speA/plaP double mutant was grown in the presence of extracellular putrescine, the intracellular levels of putrescine were greatly reduced compared with the speA mutant alone,
indicating that PlaP functioned as the primary putrescine importer. In urothelial cell invasion assays, a speA mutant exhibited a 50% reduction in invasion when compared with wild type, and this defect could be restored by putrescine in a PlaP-dependent manner. The putrescine analog Triamide-44 partially inhibited the uptake of putrescine by PlaP and decreased both putrescine stimulated swarming and urothelial cell invasion in a speA mutant.

[254]
TÍTULO / TITLE: - Genomic profiling defines subtypes of prostate cancer with the potential for therapeutic stratification.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-12-3606
AUTORES / AUTHORS: - Schoenborn JR; Nelson PS; Fang M
INSTITUCIÓN / INSTITUTION: - Clinical Research Division, Fred Hutchinson Cancer Research Center.
RESUMEN / SUMMARY: - The remarkable variation in prostate cancer clinical behavior represents an opportunity to identify and understand molecular features that can be used to stratify patients into clinical subgroups for more precise outcome prediction and treatment selection. Significant progress has been made in recent years in establishing the composition of genomic and epigenetic alterations in localized and advanced prostate cancers using array-based technologies and next generation sequencing approaches. The results of these efforts shed new light on our understanding of this disease and point to subclasses of prostate cancer that exhibit distinct vulnerabilities to therapeutics. The goal of this review is to categorize the genomic data and, where available, corresponding expression, functional, or related therapeutic information, from recent large-scale and in-depth studies that demonstrate a new appreciation for the molecular complexity of this disease. We focus on how these results inform our growing understanding of the mechanisms that promote genetic instability, as well as routes by which specific genes and biological pathways may serve as biomarkers or potential targets for new therapies. We summarize data that indicate the presence of genetic subgroups of prostate cancers and demonstrate the high level of intra- and intertumoral heterogeneity, as well as updated information on disseminated and circulating tumor cells. The integrated analysis of all types of genetic alterations that culminate in altering critical biological pathways may serve as the impetus for developing new therapeutics, repurposing agents used currently for treating other malignancies, and stratifying early and advanced prostate cancers for appropriate interventions.

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Membranous expression of podocalyxin-like protein is an independent factor of poor prognosis in urothelial bladder cancer.

**METHODS:** Immunohistochemical PODXL expression was examined in tissue microarrays with tumours from two independent cohorts of patients with urothelial bladder cancer: n=100 (Cohort I) and n=343 (Cohort II). The impact of PODXL expression on disease-specific survival (DSS; Cohort II), 5-year overall survival (OS; both cohorts) and 2-year progression-free survival (PFS; Cohort II) was assessed.

**RESULTS:** Membranous PODXL expression was significantly associated with more advanced tumour (T) stage and high-grade tumours in both cohorts, and a significantly reduced 5-year OS (unadjusted HR=2.25 in Cohort I and 3.10 in Cohort II, adjusted HR=2.05 in Cohort I and 2.18 in Cohort II) and DSS (unadjusted HR=4.36, adjusted HR=2.70). In patients with Ta and T1 tumours, membranous PODXL expression was an independent predictor of a reduced 2-year PFS (unadjusted HR=6.19, adjusted HR=4.60) and DSS (unadjusted HR=8.34, adjusted HR=7.16).

**CONCLUSION:** Membranous PODXL expression is an independent risk factor for progressive disease and death in patients with urothelial bladder cancer.

is unknown whether AOe specifically increases the risk of lethal PCa. The objective of this study was to determine the association between AOe and the risk of detecting high-grade PCa (HGPCa) (Gleason score \( \geq 7 \)) on biopsy in a US Veteran cohort. METHODS: Risk factors included clinicodemographic and laboratory data from veterans who were referred for an initial prostate biopsy. Outcomes were defined as the presence versus the absence of PCa, HGPCa, or low-grade PCa (LGPCa) (Gleason score \( < 7 \)) in biopsy specimens. Risk among AOe veterans relative to unexposed veterans was estimated using multivariate logistic regression. Separate models were used to determine whether AOe was associated with an increased risk of PCa, HGPCa, or LGPCa.

RESULTS: Of 2720 veterans who underwent biopsy, PCa was diagnosed in 896 veterans (32.9%), and 459 veterans (16.9%) had HGPCa. AOe was associated with a 52% increase in the overall risk of detecting PCa (adjusted odds ratio, 1.52; 95% confidence interval, 1.07-2.13). AOe did not confer an increase in the risk of LGPCa (adjusted odds ratio, 1.24; 95% confidence interval, 0.81-1.91), although a 75% increase in the risk of HGPCa was observed (adjusted odds ratio, 1.75; 95% confidence interval, 1.12-2.74). AOe was associated with a 2.1-fold increase (95% confidence interval, 1.22-3.62; \( P < .01 \)) in the risk of detecting PCa with a Gleason score \( \geq 8 \).

CONCLUSIONS: The current results indicated that an increased risk of PCa associated with AOe is driven by an increased risk of HGPCa in men who undergo an initial prostate biopsy. These findings may aid in improved PCa screening for Vietnam-era veterans. Cancer 2013. © 2013 American Cancer Society.
using technetium 99mTc methylene diphosphonate at the initial staging. If the bone scan finding was equivocal, computed tomography or magnetic resonance imaging was performed to confirm the diagnosis. Age, prostate-specific antigen (PSA) at diagnosis, clinical stage assigned according to the TNM 2002 staging system and biopsy Gleason score were collected in all patients. Multivariate logistic regression analysis was performed to identify statistically significant covariates and then receiver operating characteristic (ROC) curves were generated to identify optimal cut-off values. Using these cut-off values, a formula was devised to calculate an index value for BM screening at diagnosis. The model was cross-validated using the leave-one-out method.

Results: Of the 488 patients, 65 patients (13.3%) had BM. The area under the ROC curve was 0.87 (95% confidence interval 0.83-0.94). The sensitivity of the cut-off point was 87.7% and the specificity was 73.1%. Bone scan is needed for all cT4 PCa patients, however, it is also advisable for cT1-T3 PCa patients who have a biopsy Gleason score $\leq 3 + 4$ and a PSA $> 132.1$, and for cT1-T3 patients having a Gleason score of $> = 4 + 3$ and PSA $> 44.5$. Conclusions: The regression model may help determine if bone scan is needed to detect BM from PCa at the time of diagnosis. The model was generated upon a single center experience. Further validation is needed in future studies.

[258]

- **TÍTULO / TITLE:** Androgen deprivation and high-dose radiotherapy for oligometastatic prostate cancer patients with less than five regional and/or distant metastases.

- **RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

- **REVISTA / JOURNAL:** Acta Oncol. 2013 Apr 2.

- **AUTORES / AUTHORS:** Schick U; Jorcano S; Nouet P; Rouzaud M; Vees H; Zilli T; Ratib O; Weber DC; Miralbell R

- **INSTITUCIÓN / INSTITUTION:** Department of Radiation Oncology, University Hospital of Geneva, Geneva, Switzerland.

- **RESUMEN / SUMMARY:** Background. Substantial survival may be observed with oligometastatic prostate cancer. Combining androgen deprivation (AD) and high-dose external beam radiotherapy (RT) to isolated regional or distant lesions may be proposed for these patients and the outcome of this strategy is the purpose of the present report. Material and methods. From 2003 to 2010, 50 prostate cancer patients were diagnosed with synchronous ($n = 7$) or metachronous ($n = 43$) oligometastases (OM). Among the relapsing patients, the recurrence occurred after radical prostatectomy in 33 patients and curative RT (+/- AD) in 10 patients. The median age at diagnosis was 63 years (range, 48-82). All patients underwent a bone scan and 18F-choline or 11C-acetate
PET-CT at the time of diagnosis or relapse, showing regional and/or distant nodal and bone and/or visceral metastases in 33 and 17 patients, respectively. The median delivered effective dose was 64 Gy. All but one patient received neo-adjuvant and concomitant AD. Results. After a median follow-up of 31 months (range, 9-89) the three-year biochemical relapse-free survival (bRFS), clinical failure-free survival, and overall survival rates were 54.5%, 58.6% and 92%, respectively. No grade 3 toxicity was observed. Improved bRFS was found to be significantly associated with the number of OM. The three-year bRFS was 66.5% versus 36.4% for patients with 1 and > 1 OMs (p = 0.031). A normalised total dose (NTD in 2 Gy/fraction, alpha/beta = 2 Gy) above 64 Gy was also correlated with a better three-year bRFS compared to lower doses: 65% vs. 41.8%, respectively (p = 0.005). On multivariate analysis, only the NTD > 64 Gy retained statistical significance (HR: 0.37, 95% CI 0.15-0.93).

Conclusion. Oligometastatic patients may be successfully treated with short AD and high-dose irradiation to the metastatic lesions. High dose improves bRFS. Such a treatment strategy may hypothetically succeed to prolong the failure-free interval between two consecutive AD courses.

[259]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Horn T; Ladwein B; Maurer T; Redlin J; Seitz AK; Gschwend JE; Retz M; Kubler HR

INSTITUCIÓN / INSTITUTION: - Department of Urology, Klinikum rechts der Isar, Urologische Klinik der Technischen Universität Munchen, Technische Universität Munchen, Ismaningerstrasse 22, 81675, Munich, Germany, thorn@lrz.tum.de.

RESUMEN / SUMMARY: - OBJECTIVES: To determine GFR with different methods in patients with first-line chemotherapy for advanced urothelial cancer (UC) and to evaluate the impact of these methods on the estimation of cisplatin eligibility. METHODS: A database was built retrospectively containing all patients receiving first-line chemotherapy for UC between 2001 and 2012 in one German high-volume center. GFR was calculated with the methods by Cockcroft-Gault (CG), MDRD and CKD-EPI. Measurements of creatinine clearance with timed urine collections were registered. RESULTS: A total of 166 patients were included. All methods of renal function determination yielded consistent results in terms of cisplatin eligibility for 134 patients (80.7 %) and disagreeing results for 32 patients (19.3 %). Twenty-two of these 32 patients
with borderline GFR received cisplatin-based chemotherapy. Fifteen of these 22 patients completed at least three cycles. The mean GFR in the mentioned 32 patients was 51.3, 56.2 and 54.2 ml/min with the method by CG, MDRD and CKD-EPI. Three, ten and four patients were estimated cisplatin-eligible with either method. There was a good correlation between MDRD and CKD-EPI (r² = 0.92). CG tended to underestimate GFR compared to both MDRD and CKD-EPI. Measurements of creatinine clearance showed a wide distribution in comparison with MDRD (r² = 0.002). CONCLUSIONS: The method used to determine GFR influences the estimation of cisplatin eligibility in a subset of UC patients. MDRD and CKD-EPI formulas seem most valuable, while CG tends to underestimate renal function. Using a strict cutoff of 60 ml/min may unnecessarily preclude cisplatin in some patients.

[260]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Rogers EN; Jones DZ; Kidd NC; Yeyeodu S; Brock G; Ragin C; Jackson M; McFarlane-Anderson N; Tulloch-Reid M; Sean Kimbro K; Kidd LR

INSTITUCIÓN / INSTITUTION: - Department of Pharmacology and Toxicology, University of Louisville, Louisville, KY, USA.

RESUMEN / SUMMARY: - Recent advances demonstrate a relationship between chronic/recurrent inflammation and prostate cancer (PCA). Among inflammatory regulators, toll-like receptors (TLRs) have a critical role in innate immune responses. However, it remains unclear whether variant TLR genes influence PCA risk among men of African descent. Therefore, we evaluated the impact of 32 TLR-associated single-nucleotide polymorphisms (SNPs) on PCA risk among African Americans and Jamaicans. SNP profiles of 814 subjects were evaluated using Illumina’s Veracode genotyping platform. Single and combined effects of SNPs in relation to PCA risk were assessed using age-adjusted logistic regression and entropy-based multifactor dimensionality reduction (MDR) models. Seven sequence variants detected in TLR6, TOLLIP (Toll-interacting protein), IRAK4 (interleukin-1 receptor-associated kinase 4) and IRF3 (interferon regulatory factor 3) were marginally related to PCA. However, none of these effects remained significant after adjusting for multiple hypothesis testing. Nevertheless, MDR modeling revealed a complex interaction between IRAK4 rs4251545 and TLR2 rs1898830 as a significant predictor of PCA risk among US men (permutation testing P-value=0.001). However, these findings
require further assessment and validation. Genes and Immunity advance online publication, 9 May 2013; doi:10.1038/gene.2013.22.

RESUMEN / SUMMARY: BACKGROUND AND PURPOSE: The differential diagnosis in single or oligo-brain lesions in metastatic cancer patients remains broad. Advanced imaging studies can be employed to help refine the differential and potentially guide treatment. METHODS: Case report of a 52-year-old male patient with known transitional cell carcinoma of the bladder presented with headaches, cognitive symptoms, and episodic presyncope. Brain magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), and octreotide scans were performed to evaluate the underlying etiology of his symptoms. RESULTS: MRI revealed two enhancing mass lesions in left temporal and left cerebellar locations. Both lesions were octreotide avid and MRS of the temporal lesion showed a single large lipid peak at 1.3 ppm, a small NAA peak, and a markedly increased choline:creatine ratio that was relatively characteristic for metastases. Pathology from surgical resection revealed transitional cell carcinoma of the bladder. CONCLUSIONS: Resection of both lesions revealed metastatic transitional cell carcinoma. This is the first report of octreotide scan characteristics in a patient with transitional cell carcinoma with central nervous system (CNS) metastases. The octreotide avidity of these transitional cell CNS metastases suggests the presence of somatostatin receptors that may be considered as a potential therapeutic target.

[262] TÍTULO / TITLE: Diabetes Mellitus and Prostate Cancer Risk; A Nationwide Case-Control Study within PCBaSe Sweden.  
RESUMEN / SUMMARY: BACKGROUND AND PURPOSE: The differential diagnosis in single or oligo-brain lesions in metastatic cancer patients remains broad. Advanced imaging studies can be employed to help refine the differential and potentially guide treatment. METHODS: Case report of a 52-year-old male patient with known transitional cell carcinoma of the bladder presented with headaches, cognitive symptoms, and episodic presyncope. Brain magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), and octreotide scans were performed to evaluate the underlying etiology of his symptoms. RESULTS: MRI revealed two enhancing mass lesions in left temporal and left cerebellar locations. Both lesions were octreotide avid and MRS of the temporal lesion showed a single large lipid peak at 1.3 ppm, a small NAA peak, and a markedly increased choline:creatine ratio that was relatively characteristic for metastases. Pathology from surgical resection revealed transitional cell carcinoma of the bladder. CONCLUSIONS: Resection of both lesions revealed metastatic transitional cell carcinoma. This is the first report of octreotide scan characteristics in a patient with transitional cell carcinoma with central nervous system (CNS) metastases. The octreotide avidity of these transitional cell CNS metastases suggests the presence of somatostatin receptors that may be considered as a potential therapeutic target.
BACKGROUND: Diabetes mellitus (DM) increases the risk for cancer at almost all sites, but data on the association with prostate cancer are inconsistent. METHODS: We assessed the risk of a prostate cancer diagnosis among men with type 2 (T2)DM in a nationwide population-based case-control study including 44,352 men with prostate cancer identified through the Prostate Cancer data Base Sweden (PCBaSe) between 2002 and 2006 and 221,495 age-matched men from the general population. RESULTS: Overall, the risk of prostate cancer among men with T2DM was lower than among men without T2DM [OR, 0.80; 95% confidence interval (CI), 0.76-0.85]. The risk decreased with longer disease duration and was observed across all tumor risk categories, although most clearly among men with low risk tumors (OR, 0.71; 95% CI, 0.64-0.80). The risk for prostate cancer was reduced among diabetic men on dietary treatment only (OR, 0.89; 95% CI, 0.80-0.99) but more markedly among men on oral hypoglycemic agents (OR, 0.80; 95% CI, 0.74-0.87) and insulin (OR, 0.72; 95% CI, 0.69-0.81). Obese diabetic men (BMI > 30 kg/m2) showed a reduced risk (OR, 0.72; 95% CI, 0.65-0.80) compared with men without diabetes. There was a trend of decreasing risk with increasing levels of HbA1c (P < 0.05). CONCLUSIONS: This nationwide study confirmed a reduced risk of being diagnosed with prostate cancer among men with T2DM, especially for low-risk tumors. An altered hormonal milieu is a plausible explanation, although the possibility of decreased prostate cancer detection among diabetic men cannot be ruled out. IMPACT: This is the largest study to examine the association between T2DM and prostate cancer accounting for tumor risk group and diabetes treatment. Cancer Epidemiol Biomarkers Prev; 1-8. ©2013 AACR.
BACKGROUND: In general population studies, obesity has been associated with risk of high-grade prostate cancer, but little is known about obesity and future prostate cancer risk among men with an initial benign biopsy of the prostate; a high-risk population. METHODS: Within a cohort of 6,692 men followed up after a biopsy or transurethral resection of the prostate (TURP) with benign findings, a nested case-control study was conducted of 494 prostate cancer cases and controls matched on age, race, follow-up duration, biopsy versus TURP and date of procedure. Body mass index at the time of the initial procedure was abstracted from medical records, and initial biopsy specimens were reviewed for the presence of prostatic intraepithelial neoplasia (PIN). RESULTS: Obesity was associated with the presence of PIN in the initial benign specimen [OR = 2.15; 95% confidence interval (CI) 1.13-4.11]. After adjustment for the matching variables, family history of prostate cancer, prostate-specific antigen (PSA) levels at the initial procedure, the number of PSA tests and digital rectal examinations during follow-up, obesity (OR = 1.57; 95% CI, 1.07-2.30) at the time of the initial procedure was associated with prostate cancer incidence during follow-up. Risk associated with obesity was confined to cases with follow-up less than 1,538 days, the median duration of follow-up among cases (OR = 1.95; 95% CI, 1.09-3.48). CONCLUSIONS: Obesity is associated with the presence of PIN in benign specimens and with future prostate cancer risk after an initial benign finding. Impact: Obesity may be a factor to consider when planning clinical follow-up after a benign biopsy.

Cancer Epidemiol Biomarkers Prev; 22(5); 898-904. ©2013 AACR.

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TÍTULO / TITLE: Polar biophenolics in sweet potato greens extract synergize to inhibit prostate cancer cell proliferation and in vivo tumor growth.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Gundala SR; Yang C; Lakshminarayana N; Asif G; Gupta MV; Shamsi S; Aneja R
INSTITUCIÓN / INSTITUTION: Department of Biology and.
RESUMEN / SUMMARY: Polyphenolic phytochemicals present in fruits and vegetables indisputably confer anticancer benefits upon regular consumption.
Recently, we demonstrated the growth-inhibitory and apoptosis-inducing properties of polyphenol-rich sweet potato greens extract (SPGE) in cell culture and in vivo prostate cancer xenograft models. However, the bioactive constituents remain elusive. Here, we report a bioactivity-guided fractionation of SPGE based upon differential solvent polarity using chromatographic techniques that led to the identification of a remarkably active polyphenol-enriched fraction, F5, which was ~100-fold more potent than the parent extract as shown by IC50 measurements in human prostate cancer cells. High-performance liquid chromatography-ultraviolet and mass spectrometric analyses of the seven SPGE fractions suggested varying abundance of the major phenols, quinic acid (QA), caffeic acid, its ester chlorogenic acid, and isochlorogenic acids, 4,5-di-CQA, 3,5-di-CQA and 3,4-di-CQA, with a distinct composition of the most active fraction, F5. Subfractionation of F5 resulted in loss of bioactivity, suggesting synergistic interactions among the constituent phytochemicals. Quantitative analyses revealed a ~2.6- and ~3.6-fold enrichment of QA and chlorogenic acid, respectively, in F5 and a definitive ratiometric relationship between the isochlorogenic acids. Daily oral administration of 400mg/kg body wt of F5 inhibited growth and progression of prostate tumor xenografts by ~75% in nude mice, as evidenced by tumor volume measurements and non-invasive real-time bioluminescence imaging. These data generate compelling grounds to further examine the chemopreventive efficacy of the most active fraction of SPGE and suggest its potential usefulness as a dietary supplement for prostate cancer management.
disruption. Information on the occurrence of prostate cancer was obtained through record linkages across the Icelandic Cancer Registry. We used Cox regression models with 95% confidence intervals (CI) to estimate HRs of prostate cancer by symptoms of sleep disruption. RESULTS: During follow-up, 135 men (6.4%) were diagnosed with prostate cancer. Compared with men without sleep disruption, those with problems falling and staying asleep were at significantly increased risk of prostate cancer [HR, 1.7 (95% CI, 1.0-2.9) and 2.1 (95% CI, 1.2-3.7)], respectively, with increasing sleep disruption severity. When restricted to advanced prostate cancer (≥ stage T3 or lethal disease), these associations became even stronger [HR 2.1 (95% CI, 0.7-6.2) and 3.2 (95% CI, 1.1-9.7)]. The results did not change after excluding from the analyses men who woke up during the night, indicative of nocturia, suggesting limited risk of reverse association. CONCLUSIONS: Our data suggest that certain aspects of sleep disruption may confer an increased risk of prostate cancer and call for additional, larger studies with longer follow-up times. Impact: Prostate cancer is one of the leading public health concerns in men; if confirmed in future studies, the association between sleep disruption and prostate cancer risk may open new avenues for prevention. Cancer Epidemiol Biomarkers Prev; 22(5); 872-9. ©2013 AACR.

[266]
TITULO / TITLE: Treatment of local-regional prostate cancer detected by PSA screening: benefits and harms according to prognostic factors.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Wever EM; Heijnsdijk EA; Draisma G; Bangma CH; Roobol MJ; Schroder FH; de Koning HJ
INSTITUCIÓN / INSTITUTION: Department of Public Health, Erasmus Medical Center, P.O. Box 2040, Rotterdam, 3000, CA, The Netherlands.
RESUMEN / SUMMARY: Background: Men with screen-detected prostate cancer can choose to undergo immediate curative treatment or enter into an expectant management programme. We quantified how the benefits and harms of immediate treatment vary according to the prognostic factors of clinical T-stage, Gleason score, and patient age. Methods: A microsimulation model based on European Randomized Study of Screening for Prostate Cancer data was used to predict the benefits and harms of immediate treatment versus delayed treatment of local-regional prostate cancer in men aged 55-74 years. Benefits included life-years gained and reduced probability of death from prostate cancer. Harms included lead time and probability of overdiagnosis. Results: The ratio of mean lead time to mean life-years gained ranged from 1.8 to 31.2, and
the additional number of treatments required per prostate cancer death prevented ranged from 0.3 to 11.6 across the different prognostic groups. Both harm-benefit ratios were lowest, most favourable, for men aged 55-59 years and diagnosed with moderate-risk prostate cancer. Ratios were high for men aged 70-74 years regardless of clinical T-stage and Gleason score. Conclusion: Men aged 55-59 years with moderate-risk prostate cancer are predicted to derive greatest benefit from immediate curative treatment. Immediate treatment is least favourable for men aged 70-74 years with either low-risk or high-risk prostate cancer.

[267]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - He W; Cheville JC; Sadow PM; Gopalan A; Fine SW; Al-Ahmadi HA; Chen YB; Oliva E; Russo P; Reuter VE; Tickoo SK

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.

RESUMEN / SUMMARY: - The 2004 World Health Organization classification of tumors defines epithelioid angiomyolipoma of kidney as a potentially malignant mesenchymal neoplasm with reported metastasis in approximately one-third of the cases. However, this conclusion was based primarily on individual case reports and small retrospective series. More recently reported larger series have shown varying results. We reviewed 437 consecutive renal angiomyolipomas with primary resection at three tertiary-care institutions with high nephrectomy volumes. Only tumors showing >80% epithelioid histology were included in this study. Tumors resected elsewhere and reviewed in consultation were not included. Twenty of these 437 (4.6%) were classified as epithelioid angiomyolipoma. The female to male ratio was 11:9, mean age 49.7 (range, 30-80) years, and mean tumor size 8.7 (range, 1-25) cm. Microscopic tumor necrosis was present in 10 (50%) tumors and mitotic activity (range, <1-5/10 high power fields) in 8 (40%); atypical mitoses were seen in only 1 (5%) tumor. Pleomorphic ganglion-like or multinucleated giant cells were seen in 18 (90%) tumors. With a mean follow-up of 82.5 (range, 1-356) months, seventeen patients were alive with no-evidence-of-disease at the time of last follow-up; two patients died of unrelated causes with no-evidence-of-disease, and one patient (5%) developed distant metastases. Our data, based on consecutively resected angiomyolipomas with long clinical follow-up, suggests that epithelioid angiomyolipomas constitute a small proportion of all angiomyolipomas, and the
rate of aggressive behavior among epithelioid angiomyolipomas, even when showing morphologic features previously reported to portend aggressive clinical behavior, is very low. Modern Pathology advance online publication, 19 April 2013; doi:10.1038/modpathol.2013.72.

[268]
TÍTULO / TITLE: - Biological and Statistical Approaches for Modeling Exposure to Specific Trihalomethanes and Bladder Cancer Risk.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

Enlace al texto completo (gratuito o de pago) 1093/aje/kwt009

AUTORES / AUTHORS: - Salas LA; Cantor KP; Tardon A; Serra C; Carrato A; Garcia-Closas R; Rothman N; Malats N; Silverman D; Kogevinas M; Villanueva CM

RESUMEN / SUMMARY: - Lifetime exposure to trihalomethanes (THM) has been associated with increased risk of bladder cancer. We explored methods of analyzing bladder cancer risk associated with 4 THM (chloroform, bromodichloromethane, dibromochloromethane, and bromoform) as surrogates for disinfection by-product (DBP) mixtures in a case-control study in España (1998-2001). Lifetime average concentrations of THM in the households of 686 incident bladder cancer cases and 750 matched hospital-based controls were calculated. Several exposure metrics were modeled through conditional logistic regression, including the following analyses: total THM (mug/L), cytotoxicity-weighted sum of total THM (pmol/L), 4 THM in separate models, 4 THM in 1 model, chloroform and the sum of brominated THM in 1 model, and a principal-components analysis. THM composition, concentrations, and correlations varied between areas. The model for total THM was stable and showed increasing dose-response trends. Models for separate THM provided unstable estimates and inconsistent dose-response relationships. Risk estimation for specific THM is hampered by the varying composition of the mixture, correlation between species, and imprecision of historical estimates. Total THM (mug/L) provided a proxy measure of DBPs that yielded the strongest dose-response relationship with bladder cancer risk. A variety of metrics and statistical approaches should be used to evaluate this association in other settings.

[269]
TÍTULO / TITLE: - Human ASH-1 Promotes Neuroendocrine Differentiation in Androgen Deprivation Conditions and Interferes With Androgen Responsiveness in Prostate Cancer Cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
BACKGROUND: Neuroendocrine differentiation in prostate cancer is a dynamic process associated to the onset of hormone-refractory disease in vivo. The molecular mechanisms underlying this process are poorly recognized. Our study aimed at testing in vitro the role of hASH-1, a transcription factor implicated in neuroendocrine differentiation, in the onset of neuroendocrine phenotype in prostate cancer cells. METHODS: Androgen sensitive LNCAP, androgen insensitive PC-3, and three immortalized prostate cancer cell lines were cultured in standard and androgen deprivation conditions. Expression of hASH-1 was modulated by either specific lentiviral transduction or shRNA interference. Inhibitors of WNT-11, a WNT family member associated to the development of neuroendocrine differentiation in prostate cancer, were also used. Cell viability was measured using the MTS method. Neuroendocrine phenotype was assessed by morphology, immunohistochemistry and real time PCR for several neuroendocrine markers. RESULTS: hASH-1 was up-modulated by androgen deprivation in LNCaP cells and in androgen-sensitive immortalized prostate cancer cells, and associated with the onset of a neuroendocrine phenotype. Silencing of hASH-1 prevented neuroendocrine differentiation, as did also the selective interference with the WNT-11 pathway. Moreover, hASH-1 over-expression in LNCaP cells was sufficient to promote neuroendocrine differentiation and increased cell viability at basal and androgen-deprived growth conditions. CONCLUSION: In summary, the present data support previous evidence that the acquisition of a neuroendocrine phenotype is linked to androgen responsiveness profiles and suggest a pivotal role of hASH-1 transcription factor, whose activity might be explored as a potential therapeutic target in prostate cancer, with special reference to hormone refractory disease. Prostate 9999:XX-XX. © 2013 Wiley Periodicals, Inc.
BACKGROUND: Observational studies report inconsistent associations of fat and fatty acids with prostate cancer. METHODS: We investigated associations between dietary fats and fatty acids and risk of prostate cancer in the NIH-American Association of Retired Persons (AARP) Diet and Health Study. Diet was assessed at baseline with self-administered food-frequency questionnaires. Cases were determined by linkage with state cancer registries. HR and 95% confidence intervals (CI) were estimated with Cox proportional hazards models. RESULTS: Among 288,268 men with average follow-up of nine years, 23,281 prostate cancer cases (18,934 nonadvanced and 2,930 advanced including 725 fatal cases) were identified. Total fat and mono- and polyunsaturated fat intakes were not associated with incidence of prostate cancer. Saturated fat intake was related to increased risk of advanced prostate cancer (HR Quintile 5 vs. Qunitile 1 (Q1 vs. Q5), 1.21; 95% CI, 1.00-1.46; Ptrend = 0.03) and fatal prostate cancer (HR Q5 vs. Q1, 1.47; 95% CI, 1.01-2.15; Ptrend = 0.04). alpha-Linolenic acid (ALA) intake was related to increased risk of advanced prostate cancer (HRQ5 vs. Q1, 1.17; 95% CI, 1.04-1.31; Ptrend = 0.01). Eicosapentanoic acid (EPA) intake was related to decreased risk of fatal prostate cancer (HRQ5 vs. Q1, 0.82; 95% CI, 0.64-1.04; Ptrend = 0.02). CONCLUSION: Our study suggests that the associations of fat and fatty acids differ by prostate cancer severity. Saturated fat, ALA, and EPA intakes were related to the risk of advanced or fatal prostate cancer but not to nonadvanced prostate cancer. IMPACT: Identifying factors associated with advanced prostate cancer could reduce morbidity and mortality.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary 
●●Enlace al texto completo (gratuito o de pago) 1007/s00270-013-0611-5
AUTORES / AUTHORS: Antunes AA; Carnevale FC; da Motta Leal Filho JM; Yoshinaga EM; Cerri LM; Baroni RH; Marcelino AS; Cerri GG; Srougi M
INSTITUCIÓN / INSTITUTION: Division of Urology, University of Sao Paulo Medical School, Av. Dr. Eneas de Carvalho Aguiar, 255, Sao Paulo, SP, 05403-001, Brazil.
RESUMEN / SUMMARY: PURPOSE: This study was designed to describe the clinical, laboratorial, and urodynamic findings of prostatic artery embolization
(PAE) in patients with urinary retention due to benign prostatic hyperplasia (BPH). METHODS: A prospective study of 11 patients with urinary retention due to BPH was conducted. Patients underwent physical examination, prostate specific antigen (PSA) measurement, transrectal ultrasound, and magnetic resonance imaging. International prostate symptom score (IPSS), quality of life (QoL), and urodynamic testing were used to assess the outcome before and after 1 year. RESULTS: Clinical success was 91% (10/11 patients) with a mean follow-up of 22.3 months (range, 12-41 months). At the first year follow-up, the mean IPSS score was 2.8 points (p = 0.04), mean QoL was 0.4 points (p = 0.001), mean PSA decreased from 10.1 to 4.3 ng/mL (p = 0.003), maximum urinary flow (Qmax) improved from 4.2 to 10.8 mL/sec (p = 0.009), and detrusor pressure (Pdet) decreased from 85.7 to 51.5 cm H2O (p = 0.007). Before PAE, Bladder Outlet Obstruction Index (BOOI) showed values >40 in 100% of patients. After PAE, 30% of patients were >40 (obstructed), 40% were between 20 and 40 (undetermined), and 30% were <20 (unobstructed). Patients with a BOOI <20 had higher PSA values at 1-day after PAE. CONCLUSIONS: Clinical and urodynamic parameters improved significantly after PAE in patients with acute urinary retention due to BPH. Total PSA at day 1 after PAE was higher in patients with unobstructed values in pressure flow studies.

[272]
TÍTULO / TITLE: - Production of Cyr61 protein is modulated by extracellular acidification and PI3K/Akt signaling in prostate carcinoma PC-3 cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.fct.2013.04.035
AUTORES / AUTHORS: - Lee YJ; Lee DM; Lee SH
INSTITUCIÓN / INSTITUTION: - Division of Molecular Cancer Research, Soonchunhyang Medical Research Institute, Soonchunhyang University, Cheonan 330-930, Republic of Korea.
RESUMEN / SUMMARY: - High expression of Cyr61, an extracellular cysteine-rich heparin-binding protein, has been associated with a malignant cell phenotype and poor outcome in prostate cancers. Although Cyr61 was found by us to be overproduced in androgen-independent PC-3 cells treated with N-acetylcysteine (NAC), its significance is still unclear. We therefore aimed to determine how and why Cyr61 protein is overexpressed in NAC-treated cells. Here, we found that Cyr61 protein level markedly increased in cells treated with NAC at high cell seeding density. Silencing of Cyr61 by siRNA induced enhanced activity of caspase-3/7, upregulation of the proapoptotic Bok, BimL and BimS, cleavage of apoptosis hallmarkers such as Bax, PARP and caspase-3, and downregulation...
of antiapoptotic Bcl2, Bcl-xL and Mcl-1 proteins. NAC treatment caused a reduction of extracellular medium pH to acidic and an increase in Akt phosphorylation, after which the replacement with NAC-free medium returned them to control levels within 24h. Acid stimulation increased the levels of Cyr61 and p-Akt proteins, whereas it suppressed the induction of proapoptotic and antiapoptotic proteins. Overall, our data indicate that PC-3 cells overproduce Cyr61 protein via activation of the PI3K/Akt signaling as a part of the survival mechanisms under the conditions causing extracellular acidity and further cytotoxicity.

[273]  
TÍTULO / TITLE: - Genome-wide methylation analysis of prostate tissues reveals global methylation patterns of prostate cancer.  
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary  
AUTORES / AUTHORS: - Luo JH; Ding Y; Chen R; Michalopoulos G; Nelson J; Tseng G; Yu YP  
INSTITUCIÓN / INSTITUTION: - Department of Pathology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.  
RESUMEN / SUMMARY: - Altered genome methylation is a hallmark of human malignancies. In this study, high-throughput analyses of concordant gene methylation and expression events were performed for 91 human prostate specimens, including prostate tumor (T), matched normal adjacent to tumor (AT), and organ donor (OD). Methylated DNA in genomic DNA was immunoprecipitated with anti-methylcytidine antibodies and detected by Affymetrix human whole genome SNP 6.0 chips. Among the methylated CpG islands, 11,481 islands were found located in the promoter and exon 1 regions of 9295 genes. Genes (7641) were methylated frequently across OD, AT, and T samples, whereas 239 genes were differentially methylated in only T and 785 genes in both AT and T but not OD. Genes with promoter methylation and concordantly suppressed expression were identified. Pathway analysis suggested that many of the methylated genes in T and AT are involved in cell growth and mitogenesis. Classification analysis of the differentially methylated genes in T or OD produced a specificity of 89.4% and a sensitivity of 85.7%. The T and AT groups, however, were only slightly separated by the prediction analysis, indicating a strong field effect. A gene methylation prediction model was shown to predict prostate cancer relapse with sensitivity of 80.0% and specificity of 85.0%. These results suggest methylation patterns useful in predicting clinical outcomes of prostate cancer.
BACKGROUND: Few randomised studies have compared antiandrogen intermittent hormonal therapy (IHT) with continuous maximal androgen blockade (MAB) therapy for advanced prostate cancer (PCa). OBJECTIVE: To determine whether overall survival (OS) on IHT (cyproterone acetate; CPA) is noninferior to OS on continuous MAB. DESIGN, SETTING, AND PARTICIPANTS: This phase 3 randomised trial compared IHT and continuous MAB in patients with locally advanced or metastatic PCa. INTERVENTION: During induction, patients received CPA 200mg/d for 2 wk and then monthly depot injections of a luteinising hormone-releasing hormone (LHRH; triptoreline 11.25mg) analogue plus CPA 200mg/d. Patients whose prostate-specific antigen (PSA) was <4 ng/ml after 3 mo of induction treatment were randomised to the IHT arm (stopped treatment and restarted on CPA 300mg/d monotherapy if PSA rose to >/=20 ng/ml or they were symptomatic) or the continuous arm (CPA 200mg/d plus monthly LHRH analogue). OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Primary outcome measurement was OS. Secondary outcomes included cause-specific survival, time to subjective or objective progression, and quality of life. Time off therapy in the intermittent arm was recorded. RESULTS AND LIMITATIONS: We recruited 1045 patients, of which 918 responded to induction therapy and were randomised (462 to IHT and 456 to continuous MAB). OS was similar between groups (p=0.25), and noninferiority of IHT was demonstrated (hazard ratio [HR]: 0.90; 95% confidence interval [CI], 0.76-1.07). There was a trend for an interaction between PSA and treatment (p=0.05), favouring IHT over continuous therapy in patients with PSA </=1 ng/ml (HR: 0.79; 95% CI, 0.61-1.02). Men treated with IHT reported better sexual function. Among the 462 patients on IHT, 50% and 28% of patients were off therapy for >/=2.5 yr or >5 yr.
respectively, after randomisation. The main limitation is that the length of time for the trial to mature means that other therapies are now available. A second limitation is that T3 patients may now profit from watchful waiting instead of androgen-deprivation therapy. CONCLUSIONS: Noninferiority of IHT in terms of survival and its association with better sexual activity than continuous therapy suggest that IHT should be considered for use in routine clinical practice.

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[275]
**TITULO / TITLE:** - Epstein-Barr virus-associated smooth muscle tumors after kidney transplantation: treatment and outcomes in a single center.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)
- [Enlace al texto completo (gratuito o de pago)](1111/ctr.12139)
**AUTORES / AUTHORS:** - Tan CS; Loh HL; Foo MW; Choong LH; Wong KS; Kee TY
**INSTITUCIÓN / INSTITUTION:** - Department of Renal Medicine, Singapore General Hospital, Singapore, Singapore.
**RESUMEN / SUMMARY:** - BACKGROUND: Epstein-Barr virus-associated smooth muscle tumors (EBV SMT) in adult kidney transplant recipients (KTR) are rare. The aims of this study are to document the clinical features, types of treatment given, and outcomes of KTR with EBV SMT in our institution. METHODS: Sixteen patients were identified from our institution’s databases. Patients’ survival, tumor outcome, and graft survival were compared between patients who remained on cyclosporine-based immunosuppressant and those who converted to sirolimus-based therapy. RESULTS: The median time of diagnosis was 9.4 yr after kidney transplantation, and majority of the patients had multifocal disease at the time of diagnosis. Overall, the patient survival rate was 75% over a mean follow-up period of five yr. Two patients with non-functioning allograft at the time of diagnosis of EBV SMT were excluded from the treatment outcome analysis. Comparing the sirolimus (n = 7) vs. cyclosporine groups (n = 7), patient survival rate was 100% vs. 42.9% (p = 0.08), graft survival 71.4% vs. 28.7% (p = 0.53), and disease-free status 42.9% vs. 14.3% (p = 0.73), respectively. CONCLUSION: Surgical resection in combination with decreasing immunosuppression or conversion to sirolimus appears to be effective in the treatment of EBV SMT in KTR.

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[276]
**TITULO / TITLE:** - Comment on: The national burden of infections after prostate biopsy in England and Wales: a wake-up call for better prevention.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)
**REVISTA / JOURNAL:** - J Antimicrob Chemother. 2013 Apr 30.
[277] **TÍTULO / TITLE:** - The national burden of infections after prostate biopsy in England and Wales: a wake-up call for better prevention—authors’ response. 
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary 
**REVISTA / JOURNAL:** - J Antimicrob Chemother. 2013 May 16.

[278] **TÍTULO / TITLE:** - NMIBC risk calculators: how useful are they for the practicing urologist and how can their clinical utility be improved? 
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary 

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary 
AUTORES / AUTHORS: Karami S; Daugherty SE; Schonfeld SJ; Park Y; Hollenbeck AR; Grubb RL 3rd; Hofmann JN; Chow WH; Purdue MP

RESUMEN / SUMMARY: Clinical and experimental findings suggest that female hormonal and reproductive factors could influence kidney cancer development. To evaluate this association, we conducted analyses in 2 large prospective cohorts (the National Institutes of Health-AARP Diet and Health Study (NIH-AARP), 1995-2006, and the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO), 1993-2010). Cohort-specific and aggregated hazard ratios and 95% confidence intervals relating reproductive factors and kidney cancer risk were computed by Cox regression. The analysis included 792 incident kidney cancer cases among 283,952 postmenopausal women. Women who had undergone a hysterectomy were at a significantly elevated kidney cancer risk in both NIH-AARP (hazard ratio = 1.28, 95% confidence interval: 1.09, 1.50) and PLCO (hazard ratio = 1.41, 95% confidence interval: 1.06, 1.88). Similar results were observed for both cohorts after analyses were restricted to women who had undergone a hysterectomy with or without an oophorectomy. For the NIH-AARP cohort, an inverse association was observed with increasing age at menarche (P for trend = 0.02) and increasing years of oral contraceptive use (P for trend = 0.02). No clear evidence of an association with parity or other reproductive factors was found. Our results suggest that hysterectomy is associated with increased risk of kidney cancer. The observed associations with age at menarche and oral contraceptive use warrant further investigation.

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TÍTULO / TITLE: Plasma levels of nitrate and risk of prostate cancer: a prospective study.

RESUMEN / SUMMARY: Background:Nitrate and nitrite supplements have recently been shown to improve cardiovascular health, but there is concern that these supplements could contribute to the development of cancer. Previous small, cross-sectional studies reported positive associations between circulating nitrate/nitrite levels and cancer. Prospective studies examining the association between plasma nitrate and cancer, especially prostate cancer (PCa), are lacking. Methods:We conducted a nested case-control study within
the Health Professionals Follow-up Study. Baseline blood samples were collected in 1994, and incident cases of PCa were identified from 1997-2005. Baseline plasma levels of nitrate were measured in the 630 cases and 630 matched controls. Results: We have found that baseline levels of plasma nitrate were not associated with risk of PCa. Compared to quintile 1, the relative risk from quintiles 2-5 were 1.13 (95% CI 0.78-1.63), 0.93 (95% CI 0.63-1.38), 0.95 (95% CI 0.65-1.39), and 0.99 (95% CI 0.68-1.48); p for trend was 0.9 after adjustment of multivariate risk factors. Further, plasma nitrate appeared to be inversely associated with advanced-stage PCa. The relative risk across extreme quartiles was 0.44 (95% CI 0.17-1.12; p for trend = 0.07) for the whole data set and 0.30 (95% CI 0.09-0.99; p for trend = 0.05) for the fasting data set.

Conclusions: We did not find an increased risk of PCa associated with higher plasma nitrate levels. A potential protective association between nitrate and aggressive forms of PCa requires confirmation. Impact: Nitrate-nitrite-nitric oxide pathway has emerged as a new therapeutic pathway for chronic diseases. The results of this study certainly merit replications.

[281]
TITULO / TITLE: p53 interferes with microtubule-stabilizing agent-induced apoptosis in prostate and colorectal cancer cells.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Kim JY; Chung JY; Lee SG; Kim YJ; Park JE; Yun J; Park YC; Kim BG; Yoo YH; Kim JM
INSTITUCION / INSTITUTION: Department of Anatomy and Cell Biology, Dong-A University, Busan, Republic of Korea.
RESUMEN / SUMMARY: Taxanes are microtubule-stabilizing agents that have anticancer activity against several types of human solid tumors. Although the primary mechanism of action of these drugs is well understood, the signaling pathways that confer resistance to these agents in certain types of cancer remain poorly understood. In particular, the association of p53 with the mechanism(s) of taxane-mediated cell death is still controversial. In this study, we showed that p53 has a profound inhibitory effect on docetaxel (Doc)-induced apoptosis in prostate and colorectal cancer cells and that caspases play a critical role in this process. Doc induced prostate cancer cell apoptosis at high levels in p53-null PC3 cells, at intermediate levels in p53-mutant DU145 cells and at low levels in p53 wild-type LNCaP cells. While transient overexpression of p53 in PC3 cells suppressed Doc-induced apoptosis, knockdown of p53 in LNCaP cells increased apoptosis. This finding was further confirmed using an isogenic pair of colorectal cancer cell lines, HCT-116 p53/-/
and p53+/+, indicating that p53 inhibits induction of apoptosis by Doc. To our knowledge, this is the first report describing that chemical or genetic knockout of p53 enhances the susceptibility of both prostate and colorectal cancer cells to Doc-induced apoptosis. These results may suggest an approach to stratify patients for regimens involving Doc.

[282]

TÍTULO / TITLE: Juglone, isolated from Juglans mandshurica Maxim, induces apoptosis via down-regulation of AR expression in human prostate cancer LNCaP cells.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Xu H; Yu X; Qu S; Sui D

INSTITUCIÓN / INSTITUTION: Department of Pharmacology, School of Pharmaceutical Sciences, Jilin University, 1266 Fujin Rd., Changchun, Jilin Province 130021, PR China.

RESUMEN / SUMMARY: Juglone is a natural compound which has been isolated from Juglans mandshurica Maxim. Recent studies have shown that juglone had various pharmacological effects such as anti-viral, anti-bacterial and anti-cancer. However, its anti-cancer activity on human prostate cancer LNCaP cell has not been examined. Thus, the current study was designed to elucidate the molecular mechanism of apoptosis induced by juglone in androgen-sensitive prostate cancer LNCaP cells. MTT assay was performed to examine the anti-proliferative effect of juglone. Occurrence of apoptosis was detected by Hoechst 33342 staining and flow cytometry in LNCaP cells treated with juglone for 24h. The result shown that juglone inhibited the growth of LNCaP cells in a dose-dependent manner. Morphological changes of apoptotic body formation after juglone treatment were observed by Hoechst 33342 staining. This apoptotic induction was associated with loss of mitochondrial membrane potential, and caspase-3, -9 activation. Moreover, we found that juglone significantly inhibited the expression levels of androgen receptor (AR) and prostate-specific antigen (PSA) in a dose-dependent manner, as well as abrogated up-regulation of AR and PSA genes with and/or without dihydrotestosterone (DHT). Take together, our results demonstrated that juglone might induce the apoptosis in LNCaP cell via down-regulation of AR expression. Therefore, our results indicated that juglone may be a potential candidate of drug for androgen-sensitive prostate cancer.

[283]
TÍTULO / TITLE: - Epigallocatechin-3-gallate promotes apoptosis and expression of the caspase 9 splice variant in PC3 prostate cancer cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hagen RM; Chedea VS; Mintoff CP; Bowler E; Morse HR; Ladomery MR

INSTITUCIÓN / INSTITUTION: - Centre for Research in Bioscience, Faculty of Health and Life Sciences, University of the West of England, Coldharbour Lane, Frenchay, Bristol BS16 1QY, UK.

RESUMEN / SUMMARY: - Growing evidence suggests that the flavonoid epigallocatechin-3-gallate (EGCG), notably abundant in green tea, has health-promoting properties. We examined the effect of EGCG on cell survival and apoptosis in the prostate cancer cell line PC3. Cell survival was reduced and apoptosis increased significantly with a low dose of 1 microM EGCG. The ability of the anticancer drug cisplatin to promote apoptosis was enhanced by EGCG. Furthermore, EGCG, both alone and in combination with cisplatin, promoted the expression of the pro-apoptotic splice isoform of caspase 9.

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[284]

TÍTULO / TITLE: - Ultrasonography in prostate cancer: current roles and potential applications in radiorecurrent disease.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Rosoff JS; Prasad SM; Savage SJ

INSTITUCIÓN / INSTITUTION: - Department of Urology, Medical University of South Carolina, 96 Jonathan Lucas Street CSB 644, Charleston, SC, 29425, USA, rosoff@musc.edu.

RESUMEN / SUMMARY: - The use of ultrasound technology for prostate cancer imaging has evolved over many years. In order to fully appreciate today’s application of prostate ultrasound in the primary diagnostic setting as well as for radiorecurrent prostate cancer, it is helpful to understand the progression of this technology from its inception. This review begins with a brief history of the development of ultrasonography for the prostate. This is followed by a summary of the data evaluating ultrasound in the primary diagnosis of prostate cancer. Its application in the post-treatment setting is then addressed. Finally, several emerging technologies are discussed, including contrast-enhanced ultrasound, elastography and HistoScanning. These new modalities may hold promise for
identifying incompletely ablated prostate tissue following radiation therapy or other ablative techniques.

[285]
**Título / Title:** - Re: socioeconomic status, healthcare density, and risk of prostate cancer among african american and caucasian men in a large prospective study.

**Resumen / Summary:** - Enlace al Resumen / Link to its Summary


**Autores / Authors:** - Penson DF

[286]
**Título / Title:** - Risk factors contributing to urinary protein expression resulting from bevacizumab combination chemotherapy.

**Resumen / Summary:** - Enlace al Resumen / Link to its Summary


**Autores / Authors:** - Teramachi H; Shiga H; Komada N; Tamura K; Yasuda M; Umeda M; Tachi T; Goto C; Tsuchiya T

**Institución / Institution:** - Laboratory of Clinical Pharmacy, Gifu Pharmaceutical University, Gifu, Japan. teramachih@gifu-pu.ac.jp

**Resumen / Summary:** - Proteinuria following administration of bevacizumab is reported to be a specific adverse effect, but the risk factors for proteinuria have not been elucidated. In this study, the risk factors for urinary protein expression resulting from bevacizumab combination chemotherapy were investigated. The subjects were 47 patients aged > or = 20 years who had received bevacizumab combination chemotherapy at Gifu Municipal Hospital between February 2010 and February 2011. A total of 13 patients were excluded based on exclusion criteria; of the remaining 34 patients, 24 (70.6%) were assigned to the urinary protein non-expression group, and 10 (29.4%) were assigned to the urinary protein expression group. The results of multivariate logistic regression analysis revealed a significant difference in systolic blood pressure (> or =130 mmHg) between the two groups (OR: 14.499, 95%CI: 1.326-158.577, p=0.028). This finding shows that systolic blood pressure (> or =130 mmHg) is a risk factor for urinary protein expression resulting from bevacizumab combination chemotherapy.

[287]

RESUMEN / SUMMARY: Purposes: Setup errors and prostate intrafraction motion are main sources of localization uncertainty in prostate cancer radiation therapy. This study evaluates four different imaging modalities 3D ultrasound (US), kV planar images, cone-beam computed tomography (CBCT), and implanted electromagnetic transponders (Calypso/Varian) to assess interfraction and intrafraction localization errors during intensity-modulated radiation therapy based treatment of prostate cancer. METHODS: Twenty-seven prostate cancer patients were enrolled in a prospective IRB-approved study and treated to a total dose of 75.6 Gy (1.8 Gy/fraction). Overall, 1100 fractions were evaluated. For each fraction, treatment targets were localized using US, kV planar images, and CBCT in a sequence defined to determine setup offsets relative to the patient skin tattoos, intermodality differences, and residual errors for each patient and patient cohort. Planning margins, following van Herk’s formalism, were estimated based on error distributions. Calypso-based localization was not available for the first eight patients, therefore centroid positions of implanted gold-seed markers imaged prior to and immediately following treatment were used as a motion surrogate during treatment. For the remaining 19 patients, Calypso transponders were used to assess prostate intrafraction motion. RESULTS: The means (μ), and standard deviations (SD) of the systematic (Sigma) and random errors (sigma) of interfraction prostate shifts (relative to initial skin tattoo positioning), as evaluated using CBCT, kV, and US, averaged over all patients and fractions, were: [μ CBCT = (-1.2, 0.2, 1.1) mm, Sigma CBCT = (3.0, 1.4, 2.4) mm, sigma CBCT = (3.2, 2.2, 2.5) mm], [μkV = (-2.9, -0.4, 0.5) mm, Sigma kV = (3.4, 3.1, 2.6) mm, sigma kV = (2.9, 2.0, 2.4) mm], and [μUS = (-3.6, -1.4, 0.0) mm, Sigma US = (3.3, 3.5, 2.8) mm, sigma US = (4.1, 3.8, 3.6) mm], in the anterior-posterior (A/P), superior-inferior (S/I), and the left-right (L/R) directions, respectively. In the treatment protocol, adjustment of couch was guided by US images. Residual setup errors as assessed by kV images were found to be: μ residual = (-0.4, 0.2, 0.2) mm, Sigma residual = (1.0, 1.0, 0.7) mm, and sigma residual = (2.5, 2.3, 1.8) mm. Intrafraction prostate motion, evaluated using electromagnetic transponders, was: μ intrafxn = (0.0, 0.0, 0.0) mm, Sigma intrafxn = (1.3, 1.5, 0.6) mm, and sigma intrafxn = (2.6, 2.4, 1.4) mm. Shifts between pre- and post-treatment kV images were: μ kV(post-
pre) = (-0.3, 0.8, -0.2), Sigma kV(post-pre) = (2.4, 2.7, 2.1) mm, and sigma kV(post-pre) = (2.7, 3.2, 3.1) mm. Relative to skin tattoos, planning margins for setup error were within 10-11 mm for all image-based modalities. The use of image guidance was shown to reduce these margins to less than 5 mm. Margins to compensate for both residual setup (interfraction) errors as well as intrafraction motion were 6.6, 6.8, and 3.9 mm in the A/P, S/I, and L/R directions, respectively. CONCLUSIONS: Analysis of interfraction setup errors, performed with US, CBCT, planar kV images, and electromagnetic transponders, from a large dataset revealed intermodality shifts were comparable (within 3-4 mm). Interfraction planning margins, relative to setup based on skin marks, were generally within the 10 mm prostate-to-planning target volume margin used in our clinic. With image guidance, interfraction residual planning margins were reduced to approximately less than 4 mm. These findings are potentially important for dose escalation studies using smaller margins to better protect normal tissues.
were associated with a worse prognosis. Serum albumin was a predictor of mortality in logistic regression analysis. CONCLUSION: The ultimate outcome of the patients with AA amyloidosis is poor, possibly due to the late referral to the nephrology clinics. Early referral may be helpful to improve prognosis.

[289]

**TÍTULO / TITLE:** Nuclear expression of Smad proteins and its prognostic significance in clear cell renal cell carcinoma.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** Hum Pathol. 2013 May 10. pii: S0046-8177(13)00133-0. doi: 10.1016/j.humpath.2013.03.009.

●●Enlace al texto completo (gratuito o de pago) 1016/j.humpath.2013.03.009

**AUTORES / AUTHORS:** Park JH; Lee C; Suh JH; Chae JY; Moon KC

**INSTITUCIÓN / INSTITUTION:** Department of Pathology, Seoul National University College of Medicine, Seoul 110-799, South Korea.

**RESUMEN / SUMMARY:** Smad2, Smad3, and Smad4 are components of the transforming growth factor beta signaling pathway associated with tumorigenesis. The expression of these proteins is associated with tumor progression and prognosis of many cancers. This study aimed to evaluate the nuclear expression of Smad2, Smad3, and Smad4 in clear cell renal cell carcinoma and to assess the clinical significance and prognostic value of their expression patterns. The nuclear expression levels of Smads were evaluated in 637 cases of clear cell renal cell carcinomas using immunohistochemistry. To determine the statistical significance of Smad expression in clear cell renal cell carcinoma, each of the cases were divided into 2 groups (low and high expression groups) according to the extent of nuclear staining. Nuclear expressions of Smad3 and Smad4 were inversely correlated with the patient’s age, the nuclear grade, the tumor size, and the pTNM stage. The Smad3-low and Smad4-low groups showed significantly shorter cancer-specific and progression-free survival times. Furthermore, multivariate analysis showed that both Smad3 and Smad4 were independent predictors for progression-free survival (P = .008 and P = .022, respectively). However, Smad2 expression was not related to clinicopathologic parameters and patients’ survival. These results suggest that nuclear expressions of Smad3 and Smad4 were related to prognosis of clear cell renal cell carcinoma patients and may serve as novel prognostic markers in clear cell renal cell carcinoma patients.

[290]

**TÍTULO / TITLE:** Methylselenol prodrug enhances MDV3100 efficacy for treatment of castration-resistant prostate cancer.
The next-generation antiandrogen MDV3100 prolongs overall survival of patients with metastatic castration-resistant prostate cancer (CRPC). However, patient responses are variable, and survival benefit remains relatively small. Developing effective modality to improve MDV3100 efficacy is urgently needed. Recent evidence suggests that constitutively active androgen receptor splice variants (AR-Vs) drive resistance to MDV3100. In our study, we show that methylselenol prodrug downregulates the expression and activity of both the full-length AR (AR-FL) and AR-Vs. The downregulation is independent of androgen and could be attributable to repressed transcription of the AR gene. Cotreatment with methylselenol prodrug and MDV3100 suppresses AR signalling more dramatically than either agent alone, and synergistically inhibits the growth of CRPC cells in vitro. The combinatorial efficacy is observed in not only AR-V-expressing cells but also cells expressing predominantly AR-FL, likely owing to the ability of the two drugs to block the AR signaling cascade at distinct steps. Ectopic expression of AR-FL or AR-V7 attenuates the combinatorial efficacy, indicating that downregulating AR-FL and AR-V7 is importantly involved in mediating the combinatorial efficacy. Significantly, methylselenol prodrug also downregulates AR-FL and AR-Vs in vivo and substantially improves the antitumor efficacy of MDV3100. These findings support a potential combination therapy for improving MDV3100 efficacy, and provide a rationale for evaluating the clinical application of combining methylselenol prodrug with MDV3100 for the treatment of CRPC.
INSTITUCIÓN / INSTITUTION: - Department of Endocrinology, Monash Health, Monash Medical Centre, Clayton, Australia; Bone Joint and Cancer Unit, Prince Henry’s Institute, Block E, Level 4, Monash Medical Centre, Clayton, Australia; Department of Medicine, Southern Clinical School, Monash University, Clayton, Australia. Electronic address: fran.milat@princehenrys.org.

RESUMEN / SUMMARY: - Prostate cancer is a leading cause of cancer death, frequently associated with widespread bone metastases. We report two cases of hypocalcemia following the first dose of denosumab in metastatic hormone refractory prostate cancer, the first case requiring 26 days of intravenous calcium therapy. This is the first report of prolonged hypocalcemia following denosumab in a patient with normal renal function.


AUTORES / AUTHORS: - Arantes-Rodrigues R; Pinto-Leite R; Ferreira R; Neuparth MJ; Pires MJ; Gaivao I; Palmeira C; Santos L; Colaco A; Oliveira P

INSTITUCIÓN / INSTITUTION: - Department of Veterinary Sciences, CECAV, University of Tras-os-Montes and Alto Douro, Vila Real, Portugal.

RESUMEN / SUMMARY: - To assess the efficacy of meloxicam, a non-steroidal anti-inflammatory drug (NSAID), on three human urinary bladder cancer cell lines (HT1376, T24 and 5637) and on mice urinary bladder cancer chemically induced by N-butyl-N-(4-hydroxybutyl) nitrosamine (BBN). The in vitro effects of meloxicam were assessed by optical microscopy, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) method, flow cytometry and comet assay. In vivo, Hsd:ICR male mice were exposed to BBN in drinking water, over the course of 12 weeks. Subsequently, animals were treated with meloxicam by intraperitoneal route, for 6 consecutively weeks. Tumour development was evaluated by haematoxylin and eosin staining. Renal and hepatic functions, interleucin-6 (IL-6), C-reactive protein (CRP) and tumour necrosis factor (TNFalpha) were also evaluated. In vitro, meloxicam induced a significant (P<0.05) decrease of cell proliferation. A significant (P<0.05) cell cycle arrest on G0/G1 phase was also detected in all the cell lines, with a slight but significant increase of sub-G0/G1 fraction on T24 (P=0.006) and 5637 (P<0.001) cells. Also a significant (P<0.05) increase in DNA damage was found on meloxicam-treated cells. In vivo, the incidence of pre-neoplastic lesions induced by BBN was not affected by meloxicam treatment. However, although not statistically
Meloxicam is effective on in vitro and in vivo models of urinary bladder cancer. These findings support that meloxicam deserves more attention on urinary bladder cancer study.

[293]
TÍTULO / TITLE: - The role of DAB2IP in androgen receptor activation during prostate cancer progression.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wu K; Liu J; Tseng SF; Gore C; Ning Z; Sharifi N; Fazli L; Gleave M; Kapur P; Xiao G; Sun X; Oz OK; Min W; Alexandrakis G; Yang CR; Hsieh CL; Wu HC; He D; Xie D; Hsieh JT
INSTITUCIÓN / INSTITUTION: - 1] Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA [2] Department of Urology, The First Affiliated Hospital, Medical School of Xi’an Jiaotong University, Xi’an, Shaanxi, China.
RESUMEN / SUMMARY: - Altered androgen-receptor (AR) expression and/or constitutively active AR are commonly associated with prostate cancer (PCa) progression. Targeting AR remains a focal point for designing new strategy of PCa therapy. Here, we have shown that DAB2IP, a novel tumor suppressor in PCa, can inhibit AR-mediated cell growth and gene activation in PCa cells via distinct mechanisms. DAB2IP inhibits the genomic pathway by preventing AR nuclear translocation or phosphorylation and suppresses the non-genomic pathway via its unique functional domain to inactivate c-Src. Also, DAB2IP is capable of suppressing AR activation in an androgen-independent manner. In addition, DAB2IP can inhibit several AR splice variants showing constitutive activity in PCa cells. In DAB2IP-/- mice, the prostate gland exhibits hyperplastic epithelia, in which AR becomes more active. Consistently, DAB2IP expression inversely correlates with AR activation status particularly in recurrent or metastatic PCa patients. Taken together, DAB2IP is a unique intrinsic AR modulator in normal cells, and likely can be further developed into a therapeutic agent for PCa. Oncogene advance online publication, 22 April 2013; doi:10.1038/onc.2013.143.

[294]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
BACKGROUND: Benign prostatic hyperplasia (BPH) is a common disease prevalent in elderly men. However, the genetic determinants of BPH remain unclear. Because BPH and prostate cancer (PCa) share some common pathological characteristics, we investigated whether susceptibility loci for PCa contributed to BPH risk and BPH aggressiveness in Chinese men.

METHODS: Fourteen SNPs associated with PCa risk in a Chinese population were genotyped in 426 BPH cases (184 aggressive and 242 non-aggressive BPH cases) and 1,008 controls. The association between the SNPs and BPH risk/aggressiveness was estimated using logistic regression analysis. In addition, effects of the 14 SNPs on BPH related clinical traits, including International Prostate Symptom Score (IPSS), prostate volume, total PSA, and free PSA were evaluated using linear regression analysis.

RESULTS: Two SNPs, rs12621278 in ITGA6 at 2q31 (OR = 0.82, P = 0.05) and rs339331 in RFX6 at 6q22 (OR = 1.22, P = 0.04) were significantly associated with BPH. In addition, rs12621278 (OR = 0.73, P = 0.05) and rs12653946, 13 kb upstream of IRX4 at 5p15 (OR = 1.40, 0.03), were significantly associated with aggressive BPH. Moreover, the risk allele of rs12621278 (G) and rs12653946 (T) for aggressive BPH were significantly associated with elevated IPSS after treatment (P = 0.01).

CONCLUSIONS: This is the first systematic investigation on the contributions of PCa susceptibility loci to risk and aggressiveness of BPH. Our findings advance our understanding of the genetic basis of BPH, especially aggressive BPH. In addition, our results provide new insights into the genetic determinants shared between BPH and PCa.

[295]

TÍTULO / TITLE: Monocyte chemotactic protein-1 and CC chemokine receptor 2 polymorphisms and prognosis of renal cell carcinoma.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Liu GX; Zhang X; Li S; Koiiche RD; Sindsceii JH; Song H
INSTITUCIÓN / INSTITUTION: - Department of Nephrology, Huizhou Municipal Central Hospital, 41 E Ling Bei Road, Huizhou, Guangdong, 516001, China, guanxian_liu@126.com.

RESUMEN / SUMMARY: - Monocyte chemoattractant protein-1 (MCP-1) and its receptor CC chemokine receptor 2 (CCR2) play a major role in inflammation and proliferation of cancers. We investigated a possible association between polymorphisms in MCP-1 and CCR2 genes (MCP-1 -2518<sup>G</sup>/G and CCR2 190G/A or V64I) and the risk as well as prognosis of renal cell carcinoma (RCC). Genotypes were determined by polymerase chain reaction-restriction fragment length polymorphism in 416 RCC cases and 458 age-matched healthy controls. Frequency of MCP-1 -2518GG genotype for cases and controls was 0.384 and 0.286, respectively; individuals carrying the GG genotype had a 1.89-fold increased risk of RCC than those with AA genotype (95 % confidence interval [CI] 1.24-2.81, p = 0.002; data were adjusted for age and sex).

Frequency of CCR2 190AA (64I/64I) genotype for cases and controls was 0.175 and 0.076, respectively; subjects having AA genotype had a 2.68-fold increased risk of RCC compared to those with the wild-type GG genotype (95 %CI 1.71-4.17, p = 4.3 x 10^-6; data were adjusted for age and sex). When analyzing the survival rate of RCC, patients with MCP-1 -2518GG genotype revealed significantly shorter survival time compared to cases with MCP-1 -2518AA and AG genotypes (p = 0.003). Similarly, RCC cases carrying CCR2 190AA genotype showed significantly shorter survival rate than patients with GG or GA genotypes (p < 0.001). These data suggested that MCP-1 -2518<sup>G</sup>/G and CCR2 190G/A polymorphisms are new risk factors for RCC and could be used as prognostic markers for this malignancy.

[296]

TÍTULO / TITLE: - Management of high-risk prostate cancer: Radiation therapy and hormonal therapy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Nomiya T; Tsuji H; Toyama S; Maruyama K; Nemoto K; Tsujii H; Kamada T

INSTITUCIÓN / INSTITUTION: - National Institute for Radiological Sciences, 4-9-1, Anagawa, Inage-ku, Chiba 263-8555, Japan. Electronic address: t_nomiya@nirs.go.jp.

RESUMEN / SUMMARY: - The prognosis of high-risk prostate cancer is poor with a high mortality rate. The Radiation Therapy Oncology Group (RTOG) has performed dose-escalation studies of external beam radiation therapy (EBRT) and has developed high-precision radiation therapy (RT) methods such as
intensity-modulated RT, carbon ion therapy, and proton beam therapy. High-dose rate brachytherapy (HDR-BT) is also studied as an option for high-risk prostate cancer treatment. Past clinical trials have suggested that the local control rate of high-risk prostate cancer improves with total EBRT dose, even for doses >70Gy. Several randomized controlled trials, including RTOG 94-06, have shown significantly better prognoses with higher doses (>75Gy) than with lower doses (<70Gy). A proton beam therapy trial (PROG 95-09) also showed similar results. A phase II clinical trial (National Institute for Radiological Sciences, Japan; trial 9904) showed that carbon ion therapy resulted in very good biochemical recurrence-free survival rates among high-risk prostate cancer patients, demonstrating particle therapy to be a valid treatment option. RTOG 86-10 showed that short-term neo-adjuvant hormonal therapy (HT) was inadequate for high-risk prostate cancer but effective for intermediate-risk prostate cancer, whereas RTOG 92-02 and the European Organisation for Research and Treatment of Cancer (EORTC) 22863 showed significant improvements in the prognosis of high-risk groups receiving long-term (>2years) HT combined with definitive RT. Further studies are warranted to elucidate optimal irradiation doses, HT treatment durations, and combination therapy schedules.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Anagnostopoulou V; Pediaditakis I; Alkahtani S; Alarifi SA; Schmidt EM; Lang F; Gravanis A; Charalampopoulos I; Stournaras C
INSTITUCIÓN / INSTITUTION: - Departments of Biochemistry (V.A., C.S.) and Pharmacology (I.P., A.G., I.C.), University of Crete Medical School, GR-71003 Heraklion, Greece; Foundation of Research and Technology (IESL-FORTH) (I.P., A.G.), Heraklion, Greece; Department of Zoology (S.A., S.A.A.), Science College, King Saud University, Riyadh, Saudi Arabia; and Department of Physiology (E.-M.S., F.L., C.S.), University of Tubingen, Tubingen, Germany.
RESUMEN / SUMMARY: - Tumor growth is fostered by inhibition of cell death, which involves the receptiveness of tumor to growth factors and hormones. We have recently shown that testosterone exerts proapoptotic effects in prostate and colon cancer cells through a membrane-initiated mechanism. In addition, we have recently reported that dehydroepiandrosterone (DHEA) can control cell fate, activating nerve growth factor (NGF) receptors, namely tropomyosin-related kinase (Trk)A and p75NTR, in primary neurons and in PC12 tumoral
cells. NGF was recently involved in cancer cell proliferation and apoptosis. In the present study, we explored the cross talk between androgens (testosterone and DHEA) and NGF in regulating apoptosis of prostate and colon cancer cells. DHEA and NGF strongly blunted serum deprivation-induced apoptosis, whereas testosterone induced apoptosis of both cancer cell lines. The antiapoptotic effect of both DHEA and NGF was completely reversed by testosterone. In line with this, DHEA or NGF up-regulated, whereas testosterone down-regulated, the expression of TrkA receptor. The effects of androgens were abolished in both cell lines in the presence of TrkA inhibitor. DHEA induced the phosphorylation of TrkA and the interaction of p75NTR receptor with its effectors, RhoGDI and RIP2. Conversely, testosterone was unable to activate both receptors. Testosterone acted as a DHEA and NGF antagonist, by blocking the activation of both receptors by DHEA or NGF. Our findings suggest that androgens may influence hormone-sensitive tumor cells via their cross talk with NGF receptors. The interplay between steroid hormone and neurotrophins signaling in hormone-dependent tumors offers new insights in the pathophysiology of these neoplasias.

[298]

TÍTULO / TITLE: - Proteolytic cleavage and truncation of NDRG1 in human prostate cancer cells, but not normal prostate epithelial cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ghalayini MK; Dong Q; Richardson DR; Assinder SJ
RESUMEN / SUMMARY: - N-myc downstream regulated gene-1 (NDRG1) is a metastasis suppressor that is down-regulated in prostate cancer. NDRG1 phosphorylation is associated with inhibition of metastasis and western blots indicate two bands at ~41 and ~46 kDa. Previous investigations by others suggest the higher band is due to NDRG1 phosphorylation. However, the current study using a dephosphorylation assay and the Phos-tag SDS-PAGE assay, demonstrated the 46 kDa NDRG1 protein band was not due to phosphorylation. Further experiments showed the NDRG1 protein bands were not affected upon glycosidase treatment, despite marked effects of these enzymes on the glycosylated protein, fetuin. Analysis using RT-PCR demonstrated only a single amplicon, and thus, the two bands could not result from an alternatively spliced NDRG1 transcript. Western blot analysis of prostate cancer cell lysates identified the 41 kDa band to be a truncated form of NDRG1, with mass spectrometry confirming the full and truncated proteins to be NDRG1. Significantly, this truncated protein was not present in normal human prostate epithelial cells. Western blot analysis using anti-NDRG1 raised to its N-terminal sequence failed to detect the truncated protein, suggesting it lacked N-
terminus amino acids (residues 1-49). Sequence analysis predicted a pseudotrypsin protease cleavage site between Cys49-Gly50. Such cleavage of NDRG1 in cancer cells may result in loss of NDRG1 tumour suppressive activity.

[299]

TÍTULO / TITLE: - Genistein downregulates onco-miR-1260b and inhibits Wnt-signalling in renal cancer cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hirata H; Ueno K; Nakajima K; Tabatabai ZL; Hinoda Y; Ishii N; Dahiya R

INSTITUCIÓN / INSTITUTION: - Department of Urology, San Francisco Veterans Affairs Medical Center and University of California at San Francisco, 4150 Clement Street San Francisco, CA 94121, USA.

RESUMEN / SUMMARY: - Background: Wnt-signalling has an important role in renal cancer and it is modulated by genistein in other cancers. Recently, microRNAs (miRNAs) have emerged as new regulators of gene expression. Thus, we focused on miRNAs to examine the regulatory mechanism of genistein on the Wnt-signalling pathway in renal cell carcinoma (RCC). Methods: Initially, we investigated the effect of genistein on Wnt-signalling (TOPflash reporter assay (TCF reporter assays)) in renal cancer cells, and using microarray identified candidate miRNAs whose expression was decreased by genistein. We performed functional analyses and investigated the relationship between miRNA expression and renal cancer patient outcomes. We also did 3'UTR luciferase assays to look at direct miRNA regulation of Wnt-signalling-related genes. Results: Genistein promoted apoptosis while inhibiting RCC cell proliferation and invasion. Genistein also decreased TCF reporter activity in RCC cells. We found that miR-1260b was highly expressed and significantly downregulated by genistein in RCC cells. The expression of miR-1260b was significantly higher in renal cancer tissues compared with normal, and significantly related to overall shorter survival. In addition, miR-1260b promoted renal cancer cell proliferation and invasion in RCC cells. The 3'UTR luciferase activity of target genes (sFRP1, Dkk2, Smad4) was significantly decreased and their protein expression significantly upregulated in miR-1260b inhibitor-transfected renal cancer cells. Conclusion: Our data suggest that genistein inhibited Wnt-signalling by regulating miR-1260b expression in renal cancer cells.
**TÍTULO / TITLE:** Phase II study of lutetium-177 labeled anti-prostate-specific membrane antigen (PSMA) monoclonal antibody J591 for metastatic castration-resistant prostate cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** Clin Cancer Res. 2013 May 28.

**AUTORES / AUTHORS:** Tagawa ST; Milowsky MI; Morris MJ; Vallabhajosula S; Christos PJ; Akhtar NH; Goldsmith SJ; Osborne J; Larson SM; Pandit-Taskar N; Scher HI; Bander NH; Nanus DM

**INSTITUCIÓN / INSTITUTION:** Medicine:Hematology/Oncology and Urology, Weill Cornell Medical College.

**RESUMEN / SUMMARY:** PURPOSE: To assess the efficacy of a single infusion of radiolabeled anti-prostate specific membrane antigen monoclonal antibody J591 (177Lu-J591) by PSA decline, measurable disease response, and survival EXPERIMENTAL DESIGN: In this dual-center phase II study, 2 cohorts with progressive metastatic castration-resistant prostate cancer received one dose of 177Lu-J591 (15 patients at 65 mCi/m2, 17 at 70 mCi/m2) with radionuclide imaging. Expansion cohort (n=15) received 70 mCi/m2 to verify response rate and examine biomarkers RESULTS: 47 patients who progressed after hormonal therapies (55.3% also received prior chemotherapy) received 177Lu-J591. 10.6% experienced > 50% decline in PSA, 36.2% experienced > 30% decline, and 59.6% experienced any PSA decline following their single treatment. One of 12 with measurable disease experienced a partial radiographic response (8 with stable disease). Sites of prostate cancer metastases were targeted in 44 of 47 (93.6%) as determined by planar imaging. All experienced reversible hematologic toxicity with grade 4 thrombocytopenia occurring in 46.8% (29.8% received platelet transfusions) without significant hemorrhage. 25.5% experienced grade 4 neutropenia with 1 episode of febrile neutropenia. The phase I maximum tolerated dose (70 mCi/m2) resulted in more 30% PSA declines (46.9% vs 13.3%, p=0.048) and longer survival (21.8 vs 11.9 months, p=0.03), but also more grade 4 hematologic toxicity and platelet transfusions. No serious non-hematologic toxicity occurred. Those with poor PSMA imaging were less likely to respond CONCLUSIONS: A single dose of 177Lu-J591 was well-tolerated with reversible myelosuppression. Accurate tumor targeting and PSA responses were seen with evidence of dose-response. Imaging biomarkers appear promising.

**TÍTULO / TITLE:** Favourable long-term outcomes with brachytherapy-based regimens in men ≤60 years with clinically localized prostate cancer.

[300] [301]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1111/j.1464-410X.2012.11769.x
AUTORES / AUTHORS: - Edwards A; Laing R; Langley S
INSTITUCIÓN / INSTITUTION: - Department of Oncology, Royal Surrey County Hospital, Guildford, Surrey, UK. albert@doctors.org.uk.

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[302]

TÍTULO / TITLE: - Favourable long-term outcomes with brachytherapy-based regimens in men <=60 years with clinically localized prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1111/j.1464-410X.2012.11663.x
AUTORES / AUTHORS: - Kollmeier MA; Fidaleo A; Pei X; Cohen G; Zaider M; Mo Q; Cox B; Yamada Y; Zelefsky MJ
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.
RESUMEN / SUMMARY: - WHAT’S KNOWN ON THE SUBJECT? AND WHAT DOES THE STUDY ADD?: Brachytherapy (BT)-based treatment for clinically localized prostate cancer is a well-accepted treatment strategy; however, there is concern that long-term outcomes and morbidity may not be acceptable in young patients (<=60 years). We report our long-term experience with BT in men aged <= 60 years with a minimum of 2 years of post-treatment follow-up. Our results show low treatment-related morbidity and excellent long-term outcomes with BT-based treatment and suggest that such treatment should be offered to this patient population. OBJECTIVE: To report long-term outcomes of men <=60 years treated with brachytherapy (BT) for low- and intermediate-risk prostate cancer. PATIENTS AND METHODS: Of 1655 patients treated with BT for clinically localized prostate cancer between January 1998 and May 2008 at Memorial Sloan-Kettering Cancer Center, 236 patients with National Comprehensive Cancer Network low- (n = 178) or intermediate-risk (n = 58) prostate cancer were <=60 years old with a 3-year minimum follow-up, and represent the subjects of this report. Brachytherapy was given either as monotherapy (n = 169) or with external beam radiation therapy (EBRT; n = 67). Forty-four patients (19%) received neoadjuvant cytoreductive hormone therapy. The ‘nadir+2’ definition was used for prostate-specific antigen (PSA) recurrence. Common Terminology Criteria for Acute Events (CTCAE) v 3.0 was used to grade genitourinary (GU) and gastrointestinal (GI) toxicity. Potency was...
defined as the ability to obtain an erection suitable for intercourse or an International Index of Erectile Function score \( \geq 22 \). The Kaplan-Meier method and Cox regression were used for statistical analysis. The median follow-up was 83 months. RESULTS: The 8-year PSA relapse-free survival (RFS), cancer-specific and overall survival rates for the entire cohort were 96, 99 and 96%, respectively. For patients with low-risk disease, the 8-year PSA RFS rate was 97% and for intermediate-risk patients it was 94% (\( P = 0.34 \)). There was no difference in PSA RFS between BT alone and combined therapy (\( P = 0.17 \)). Late grade \( \geq 2 \) GU and GI toxicity was 14 and 3%, respectively. Of 150 patients potent before treatment, 76 (51%) were potent at last follow-up, with 50/76 (66%) using no medication. There was no significant difference in post-treatment potency between BT alone and BT with EBRT (\( P = 0.74 \)). CONCLUSIONS: Brachytherapy provides patients aged \( \leq 60 \) years with low- and intermediate-risk prostate cancer with excellent outcomes and has a low risk of significant long-term GU or GI morbidity. Erectile function is preserved in >50% of patients and the majority do not require erectile dysfunction medication.

[TITULO / TITLE: - Plasma phospholipid fatty acids, dietary fatty acids and prostate cancer risk.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Bassett JK; Severi G; Hodge AM; Macinnis RJ; Gibson RA; Hopper JL; English DR; Giles GG
INSTITUCION / INSTITUTION: - Cancer Epidemiology Centre, Cancer Council Victoria, Carlton, VIC, Australia.
RESUMEN / SUMMARY: - Animal and experimental studies have demonstrated that long-chain n-3 fatty acids inhibit the development of prostate cancer, whereas n-6 fatty acids might promote it. We performed a case-cohort analysis within the Melbourne Collaborative Cohort Study using a random sample of 1,717 men and 464 prostate cancer cases to investigate associations between fatty acids assessed in plasma phospholipids (PPLs) or diet (estimated using a 121-item food frequency questionnaire) and prostate cancer risk. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox regression. Prostate cancer risk was positively associated with %PPL saturated fatty acids (SFAs); HR [95% CI] = 1.51 [1.06, 2.16] (Q5 vs. Q1, fifth vs. first quintile); \( p \)-trend = 0.003. HRs (Q5 to Q2 vs. Q1) were significantly elevated for %PPL palmitic acid. %PPL oleic acid was inversely associated with risk, HR = 0.62 [0.43, 0.91] (Q5 vs. Q1); \( p \)-trend = 0.04. No statistically significant linear trends were observed for dietary intakes. The HRs were elevated for moderate intakes.
of linoleic acid (Q2 and Q3 vs. Q1, 1.58 [1.10, 2.28] and 1.70 [1.18, 2.46], respectively), but the increase was not significant for higher intakes (Q4 and Q5). No association varied significantly by tumour aggressiveness (all p-homogeneity > 0.1). Prostate cancer risk was positively associated with %PPL SFA, largely attributable to palmitic acid and inversely associated with %PPL monounsaturated fatty acids, largely attributable to oleic acid. Higher risks were also observed for dietary n-6 polyunsaturated fats, primarily linoleic acid.

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[304]
TÍTULO / TITLE: - Use of denosumab in a patient with non-small-cell lung cancer and severe renal function impairment.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
    ●●Enlace al texto completo (gratuito o de pago) 1097/JTO.0b013e318284375c
AUTORES / AUTHORS: - Govaerts E; Vansteenkiste J
INSTITUCIÓN / INSTITUTION: - Respiratory Oncology Unit, Department of Pulmonology, and Leuven Lung Cancer Group, University Hospital KU Leuven, Leuven, Belgium.

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[305]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
    ●●Enlace al texto completo (gratuito o de pago) 1016/j.bbrc.2013.04.054
AUTORES / AUTHORS: - Bostrom AK; Lindgren D; Johansson ME; Axelsson H
INSTITUCIÓN / INSTITUTION: - Center for Molecular Pathology, Department of Laboratory Medicine, Lund University, Skane University Hospital, Malmo, SE-205 02 Malmo, Sweden.
RESUMEN / SUMMARY: - Clear cell renal cell carcinoma (ccRCC) is by far the most common type of kidney cancer and is characterized by loss of the tumor suppressor gene von Hippel-Lindau (VHL). ccRCC patients with metastatic disease has poor prognosis and today’s therapy is insufficient. The cytokine Transforming Growth Factor-beta (TGF-beta) has been extensively studied in tumor biology and is believed to serve a variety of functions in tumor progression. We have previously shown that inhibition of NOTCH signaling causes a reduced migratory and invasive capacity of ccRCC cells, at least partly by a cross-talk with the TGF-beta pathway. In the present study we aimed
to further clarify the role of TGF-beta signaling in ccRCC. We investigated the effects of TGF-beta pathway modulation and showed that TGF-beta inhibition attenuates the invasive capacity of ccRCC cells. By performing expression profiling we obtained a gene signature of the TGF-beta induced response in ccRCC cells. The expression analyses revealed an extensive overlap between the TGF-beta response and genes regulated by the hypoxia inducible factor (HIF). The link between the hypoxic and the TGF-beta pathways was further corroborated by functional experiments, which demonstrated that TGF-beta pathway activity was attenuated upon reintroduction of functional VHL in ccRCC.

[306]
TÍTULO / TITLE: - AKT upregulates B-Raf Ser445 phosphorylation and ERK1/2 activation in prostate cancer cells in response to androgen depletion.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago)
1016/j.yexcr.2013.05.008
AUTORES / AUTHORS: - Hong SK; Jeong JH; Chan AM; Parka JI
INSTITUCIÓN / INSTITUTION: - Department of Biochemistry, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA.
RESUMEN / SUMMARY: - Upregulated ERK1/2 activity is often correlated with AKT activation during prostate cancer (PCa) progression, yet their functional relation needs elucidation. Using androgen-deprived LNCaP cells, in which ERK1/2 activation occurs in strong correlation with AKT activation, we found that AKT-mediated B-Raf regulation is necessary for ERK1/2 activation. Specifically, in response to androgen deprivation, AKT upregulated B-Raf phosphorylation at Ser445 without affecting A-Raf or C-Raf-1. This effect of AKT was abolished by Arg25 to Ala mutation or truncating (4-129) the pleckstrin homology domain of AKT, indicating that the canonical AKT regulation is important for this signaling. Intriguingly, although a constitutively active AKT containing N-terminal myristoylation signal could sufficiently upregulate B-Raf phosphorylation at Ser445 in LNCaP cells, subsequent MEK/ERK activation still required hormone deprivation. In contrast, AKT activity was sufficient to induce not only B-Raf phosphorylation but also MEK/ERK activation in the hormone refractory LNCaP variant, C4-2. These data indicate that androgen depletion may induce MEK/ERK activation through a synergy between AKT-dependent and -independent mechanisms and that the latter may become deregulated in association with castration resistance. In support, consistent AKT-mediated B-Raf regulation was also detected in a panel of PCa lines derived from the cPten/-/-L mice before and after castration. Our results also demonstrate that
AKT regulates androgen receptor levels partly via the Raf/MEK/ERK pathway. This study reveals a novel crosstalk between ERK1/2 and AKT in PCa cells.

[307]

**TITULO / TITLE:** - Mutation Spectra of Kras and Tp53 in Urethral and Lung Neoplasms in B6C3F1 Mice Treated with 3,3',4,4'-Tetrachloroazobenzene.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](Toxicol Pathol. 2013 May 23.)
**REVISTA / JOURNAL:** - Enlace al texto completo (gratuito o de pago)
1177/0192623313491169

**AUTORES / AUTHORS:** - Bhusari S; Malarkey DE; Hong HH; Wang Y; Masinde T; Nolan M; Hooth MJ; Lea IA; Vasconcelos D; Sills RC; Hoenerhoff MJ
**INSTITUCIÓN / INSTITUTION:** - 1Cellular and Molecular Pathology Branch, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA.
**RESUMEN / SUMMARY:** - 3,3',4,4'-tetrachloroazobenzene (TCAB) is a contaminant formed during manufacture of various herbicide compounds. A recent National Toxicology Program study showed B6C3F1 mice exposed to TCAB developed a treatment-related increase in lung carcinomas in the high-dose group, and urethral carcinomas, an extremely rare lesion in rodents, in all dose groups. As the potential for environmental exposure to TCAB is widespread, and the mechanisms of urethral carcinogenesis are unknown, TCAB-induced urethral and pulmonary tumors were evaluated for alterations in critical human cancer genes, Kras and Tp53. Uroplakin III, CK20, and CK7 immunohistochemistry was performed to confirm the urothelial origin of urethral tumors. TCAB-induced urethral carcinomas harbored transforming point mutations in K-ras (38%) and Tp53 (63%), and 71% displayed nuclear TP53 expression, consistent with formation of mutant protein. Transition mutations accounted for 88% of Tp53 mutations in urethral carcinomas, suggesting that TCAB or its metabolites target guanine or cytosine bases and that these mutations are involved in urethral carcinogenesis. Pulmonary carcinomas in TCAB-exposed animals harbored similar rates of Tp53 (55%) and Kras (36%) mutations as urethral carcinomas, suggesting that TCAB may induce mutations at multiple sites by a common mechanism. In conclusion, TCAB is carcinogenic at multiple sites in male and female B6C3F1 mice through mechanisms involving Tp53 and Kras mutation.

[308]

**TITULO / TITLE:** - Lipid peroxidation and antioxidant system in erythrocytes of patients with renal cell carcinoma.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](Toxicol Pathol. 2013 May 23.)

232
AUTORES / AUTHORS: - Gerasimenko MN; Titova NM; Zukov RA; Dykhno YA; Peretoka ES
INSTITUCIÓN / INSTITUTION: - Siberian Federal University, Krasnoyarsk; V. F. Voyno-Yasenetsky Krasnoyarsk State Medical University, Russia.

RESUMEN / SUMMARY: - For evaluation lipid peroxidation and antioxidant status of red blood cells, 150 patients with locally advanced renal cell carcinoma were examined. The content of conjugated dienes, MDA, and reduced glutathione and activities of SOD, catalase, and glutathione metabolism enzymes were determined. It was found that the balance between pro- and anti-oxidants in patients with kidney cancer differed significantly from that of healthy people and little changed during the observation.

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TÍTULO / TITLE: - Bipolar plasma enucleation of the prostate vs open prostatectomy in large benign prostatic hyperplasia cases - a medium-term, prospective, randomized comparison.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Gilling PJ
INSTITUCIÓN / INSTITUTION: - Department of Urology, Tauranga Hospital, Tauranga, New Zealand.

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TÍTULO / TITLE: - Robot-assisted laparoscopic nephron sparing surgery for tumors over 4 cm: Operative results and preliminary oncologic outcomes from a multicentre French study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Masson-Lecomte A; Yates DR; Bensalah K; Vaessen C; de la Taille A; Roumiguie M; Doumerc N; Bruyere F; Soustelle L; Droupy S; Roupret M
INSTITUCIÓN / INSTITUTION: - Department of Urology, CHU Pitie Salpetriere, Assistance Publique Hopitaux de Paris, Paris, France; Universite Paris 6, Paris,
RESUMEN / SUMMARY: - OBJECTIVE: To assess operative and pathological results obtained after robot-assisted partial nephrectomy (RAPN) in renal masses over 4 cm. PATIENTS AND METHODS: Between 2007 and 2011, 220 robotic nephron-sparing surgeries (NSS) were performed at six French urology departments. Data were prospectively collected: age, BMI, pre and post-operative eGFR (MDRD), operative time (OT), warm ischemia time (WIT), estimated blood loss (EBL), length of hospital stay (LOS), Clavien complications, pathological results and oncologic outcome. Tumor complexity was assessed according to the RENAL nephrometry score. RESULTS: Overall, 54 tumors were included. Median follow up was 26 months. Median age at surgery was 62 years. Median RENAL nephrometry score was 7 (4-10). Median WIT was 23 min (10-59). Median OT and EBL were 180 min (110-425) and 100 cc (0-2500). Blood transfusion occurred in 7 cases (13%). Median tumor size was 45 mm (40-70). Three patients had positive surgical margins. Median LOS was 5 days (2-28). Nine patients presented post-operative complications of which 1/3 were considered as major (Clavien IIIb). Median pre-operative and post-operative eGFR was 88 (36-136) and 75 ml/min (33-122) (p = 0.01), respectively. Two patients developed subsequent metastasis. The 2-year progression free survival (PFS) rate was 90.5%. CONCLUSION: Our results confirm that RAPN is a useful and acceptable approach for renal masses greater than 4 cm in size. When technically possible, NSS provides promising short-term cancer-specific survival rates with acceptable morbidity. Tumor size is not sufficiently discriminant enough and RENAL nephrometry score should increasingly used to describe tumor complexity.

[311]

TÍTULO / TITLE: - A dose-ranging study of cabozantinib in men with castration-resistant prostate cancer and bone metastases.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Lee RJ; Saylor PJ; Dror Michaelson M; Michael Rothenberg S; Smas ME; Miyamoto DT; Gurski CA; Xie W; Maheswaran S; Haber DA; Goldin JG; Smith MR

INSTITUCIÓN / INSTITUTION: - Authors’ Affiliations: Massachusetts General Hospital Cancer Center; Dana-Farber Cancer Institute, Boston, Massachusetts; and Center for Computer Vision and Imaging Biomarkers, University of California, Los Angeles, California.
Background: Cabozantinib is an oral MET/VEGFR2 inhibitor. A recent phase II study of cabozantinib (100 mg daily) showed improved bone scans in subjects with metastatic castration-resistant prostate cancer (mCRPC), but adverse events (AE) caused frequent dose reductions. This study was designed to determine the efficacy and tolerability of cabozantinib at lower starting doses. EXPERIMENTAL DESIGN: An adaptive design was used to determine the lowest active daily dose among 60, 40, and 20 mg. The primary endpoint was week 6 bone scan response, defined as >/=30% decrease in bone scan lesion area. The secondary endpoint was change in circulating tumor cells (CTC). RESULTS: Among 11 evaluable subjects enrolled at 40 mg, there were 9 partial responses (PR), 1 complete response, and 1 stable disease (SD). Of 10 subjects subsequently enrolled at 20 mg, there were 1 PR, 5 SDs, and 4 with progressive disease. Among 13 subjects enrolled on the 40 mg expansion cohort, there were 6 PRs and 7 SDs. No subjects required dose reduction or treatment interruption at 6 or 12 weeks; 3 subjects at dose level 0 discontinued due to AEs by 12 weeks. At 40 mg, median treatment duration was 27 weeks. 58% of subjects with >/=5 CTCs/7.5mL at baseline converted to <5. CONCLUSIONS: Cabozantinib 40 mg daily was associated with a high rate of bone scan response. Cabozantinib 40 mg daily was associated with better tolerability than previously reported for cabozantinib 100 mg daily. These observations informed the design of phase III studies of cabozantinib in mCRPC. Clin Cancer Res; 19(11); 3088-94. ©2013 AACR.

[312]

TÍTULO / TITLE: - Capsaicin as an inducer of damage-associated molecular patterns (DAMPs) of immunogenic cell death (ICD) in human bladder cancer cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - D’Eliseo D; Manzi L; Velotti F
INSTITUCIÓN / INSTITUTION: - Department of Ecological and Biological Sciences (DEB), University of La Tuscia, Largo dell’Universita, Blocco C, 01100, Viterbo, Italy.
RESUMEN / SUMMARY: - Few conventional cytotoxic anticancer therapeutics induce immunogenic cell death (ICD). This means that they induce tumor cells to undergo apoptosis while eliciting the emission of a spatiotemporal-defined combination of damage-associated molecular patterns (DAMPs) decoded by the immune system to activate antitumor immunity effective for long-term therapeutic success. The neurotoxin capsaicin (CPS) can induce both cancer
cell apoptosis and immune-mediated tumor regression. In the present study, we investigated whether CPS is capable of eliciting the emission of ICD hallmarks in human bladder cancer cell lines undergoing apoptosis. We demonstrated that CPS induces pre- and early apoptotic cell surface exposure of calreticulin (CRT), HSP90, and HSP70 as well as ATP release. Moreover, CRT exposure was prevented by inhibition of endoplasmic reticulum-Golgi traffic by brefeldin A. Furthermore, high-mobility group box 1, HSP90, and HSP70 were passively released at late apoptotic stages. We provide the first evidence that CPS is an inducer of ICD hallmarks, suggesting CPS as a novel potential immunogenic cytotoxic agent.
RNA pol II). CONCLUSIONS: This work defines methylation landscapes of PCa according to GS, and suggests that initiating genetic events may influence the PCa epigenome which is further perturbed as PCa progresses. Moreover, CpG islands with silent chromatin signatures in benign cells are particularly susceptible to PCa related hypermethylation.

[314]

TÍTULO / TITLE: - Genome-wide association study identifies a region on chromosome 11q14.3 associated with late rectal bleeding following radiation therapy for prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Kerns SL; Stock RG; Stone NN; Blacksburg SR; Rath L; Vega A; Fachal L; Gomez-Caamaño A; De Ruyscher D; Lammering G; Parliament M; Blackshaw M; Sia M; Cesaretti J; Terk M; Hixson R; Rosenstein BS; Ostrer H

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Mount Sinai School of Medicine, New York, United States; Department of Pathology, Albert Einstein College of Medicine, Bronx, United States.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: Rectal bleeding can occur following radiotherapy for prostate cancer and negatively impacts quality of life for cancer survivors. Treatment and clinical factors do not fully predict rectal bleeding, and genetic factors may be important. MATERIALS AND METHODS: A genome-wide association study (GWAS) was performed to identify SNPs associated with the development of late rectal bleeding following radiotherapy for prostate cancer. Logistic regression was used to test the association between 614,453 SNPs and rectal bleeding in a discovery cohort (79 cases, 289 controls), and top-ranking SNPs were tested in a replication cohort (108 cases, 673 controls) from four independent sites. RESULTS: rs7120482 and rs17630638, which tag a single locus on chromosome 11q14.3, reached genome-wide significance for association with rectal bleeding (combined p-values 5.4x10^-8 and 6.9x10^-7 respectively). Several other SNPs had p-values trending toward genome-wide significance, and a polygenic risk score including these SNPs shows a strong rank-correlation with rectal bleeding (Sommers’ d=5.0x10^-12 in the replication cohort). CONCLUSIONS: This GWAS identified novel genetic markers of rectal bleeding following prostate radiotherapy. These findings could lead to the development of a predictive assay to identify patients at risk for this adverse treatment outcome so that dose or treatment modality could be modified.
[315]

**TÍTULO / TITLE:** - Re: genitourinary imaging: part 2, role of imaging in medical management of advanced renal cell carcinoma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Siegel C

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[316]

**TÍTULO / TITLE:** - Use of Testosterone Replacement Therapy in the United States and Its Effect on Subsequent Prostate Cancer Outcomes.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Kaplan AL; Hu JC

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA. Electronic address: alkaplan@mednet.ucla.edu.

**RESUMEN / SUMMARY:** - OBJECTIVE: To assess utilization trends and determine the effect of testosterone replacement therapy on outcomes in men who subsequently developed prostate cancer. METHODS: We used linked Surveillance, Epidemiology, and End Results-Medicare data to identify 149,354 men diagnosed with prostate cancer from 1992 to 2007. Of those, 2,237 men (1.5%) underwent testosterone replacement therapy before their prostate cancer diagnosis. Propensity scoring methods were used to assess cancer-specific outcomes of testosterone replacement vs no replacement therapy. RESULTS: Testosterone replacement was associated with older age at cancer diagnosis, nonwhite race, and higher comorbidity (P <.001). No testosterone vs testosterone before the prostate cancer diagnosis was associated with higher grade (34% vs 30%, P <.0001) and more T4 (6.5% vs 4.3%, P <.0001) tumors. Mortality was decreased in men with >/=2 prostate-specific antigen (PSA) tests in the year before their cancer diagnosis. No significant difference was found between groups in overall survival, cancer-specific survival, or use of salvage androgen-deprivation therapy after initial treatment. CONCLUSION: Through our observational study design, we show that testosterone use was low throughout the study period. Testosterone use was not associated with aggressive prostate cancer and did not affect overall or disease-specific
mortality. Although our findings support growing evidence that testosterone replacement is safe with respect to prostate cancer, confirmatory prospective studies are needed.

[317]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hakimi AA; Ostrovnaya I; Reva BA; Schultz N; Chen YB; Gonen M; Liu H; Takeda S; Voss MH; Tickoo SK; Reuter VE; Russo P; Cheng EH; Sander C; Motzer RJ; Hsieh JJ

INSTITUCIÓN / INSTITUTION: - Surgery: Urology Service, Memorial Sloan Kettering Cancer Center.

RESUMEN / SUMMARY: - Purpose To investigate the impact of newly identified chromosome 3p21 epigenetic tumor suppressors PBRM1, SETD2, and BAP1 on cancer specific survival (CSS) of 609 clear cell renal cell carcinoma (ccRCC) patients from two distinct cohorts. Patients and Methods Select sequencing on 3p tumor suppressors of 188 patients who underwent resection of primary ccRCC at the Memorial Sloan-Kettering Cancer Center (MSKCC) was performed to interrogate the genotype-phenotype associations. These findings were compared to analyses of the genomic and clinical dataset from our non-overlapping The Cancer Genome Atlas (TCGA) cohort of 421 primary ccRCC patients. Results 3p21 tumor suppressors are frequently mutated in both the MSKCC (PBRM1, 30.3%; SETD2, 7.4%; BAP1, 6.4%) and the TCGA (PBRM1, 33.5%; SETD2, 11.6%; BAP1, 9.7%) cohorts. BAP1 mutations are associated with worse CSS in both cohorts (MSKCC, p=0.002, HR 7.71 (2.08-28.6); TCGA, p=0.002, HR 2.21 (1.35-3.63)). SETD2 are associated with worse CSS in the TCGA cohort (p=0.036, HR 1.68 (1.04-2.73)). On the contrary, PBRM1 mutations, the second most common gene mutations of ccRCC, have no impact on CSS. Conclusion The chromosome 3p21 locus harbors three frequently mutated ccRCC tumor suppressor genes. BAP1 and SETD2 mutations (6-12%) are associated with worse CSS, suggesting their roles in disease progression. PBRM1 mutations (30-34%) do not impact CSS, implicating its principal role in the tumor initiation. Future efforts should focus on therapeutic interventions and further clinical, pathologic and molecular interrogation of this novel class of tumor suppressors.

239
Enlace al Resumen / Link to its Summary

Enlace al texto completo (gratuito o de pago) 1093/annonc/mdt130

AUTORES / AUTHORS: - Powles T; Kayani I; Sharpe K; Lim L; Peters J; Stewart GD; Berney D; Sahdev A; Chowdhury S; Boleti E; Shamash J; Reynolds AR; Jones R; Blank C; Haanen J; Bex A

INSTITUCION / INSTITUTION: - Experimental Cancer Centre, Barts Cancer Institute, Queen Mary, University of London, St Bartholomew's Hospital, London.

RESUMEN / SUMMARY: - BACKGROUND: Vascular endothelial growth factor (VEGF)-targeted therapy is administered continuously until progression in metastatic clear cell renal cancer (mRCC). The role of intermittent therapy is under investigation. Preclinical data raise concerns about this approach.

MATERIALS AND METHODS: This study combined the data from three similar phase II studies investigating VEGF-targeted therapy prior to planned nephrectomy for untreated mRCC (European Union Drug Regulating Authorities Clinical Trials 2006-004511-21, 2006-006491-38 and 2009-016675-29). The significance of progression during the planned treatment break (median 4.3 weeks) was assessed. RESULTS: Sixty-two patients had a structured treatment interruption for nephrectomy after achieving clinical benefit from treatment and restarted therapy. Twenty-three of these patients (37%) progressed (Response Evaluation Criteria In Solid Tumors v1.1) on the first scan after the treatment break. Subsequent stabilisation of disease occurred in 16 of the 23 (70%) progressing patients when the same VEGF tyrosine kinase inhibitor (TKI) was reintroduced. Baseline characteristics, such as the Memorial Sloan Kettering Cancer Centre prognostic score, did not predispose to the development of this progression. Progression during the treatment break was associated with an increased risk of death on multivariate analysis (hazard ratio (HR) 5.56; [95% confidence interval 2.29-13.5], P < 0.01). Sequential fluorodeoxyglucose positron emission tomography showed a rebound in metabolic activity during the treatment break. CONCLUSIONS: Progression during planned VEGF TKI treatment interruptions is frequent and associated with a poor prognosis. Treatment cessation should be pursued with caution.

Enlace al Resumen / Link to its Summary

Enlace al texto completo (gratuito o de pago) 1093/annonc/mdt130

AUTORES / AUTHORS: - -

INSTITUCION / INSTITUTION: -


Enlace al Resumen / Link to its Summary

RESUMEN / SUMMARY: PURPOSE: To measure quality of life (QOL) and utilities for prostate cancer (PC) patients and determine their predictors.
METHODS: A population-based, community-dwelling, geographically diverse sample of long-term PC survivors in Ontario, Canada, was identified from the Ontario Cancer Registry and contacted through their referring physician. Consenting patients completed questionnaires by mail: Health Utilities Index (HUI 2/3), Patient Oriented Prostate Utility Scale (PORPUS-U (utility), PORPUS-P (health profile), Functional Assessment of Cancer Therapy-Prostate (FACT-P), and Prostate Cancer Index (PCI). Clinical data were obtained from chart reviews. Regression models determined the effects of a series of variables on QOL and utility. RESULTS: We received questionnaires and reviewed charts for 585 patients (mean age 72.6, 2-13 years postdiagnosis). Mean utility scores were as follows: PORPUS-U = 0.92, HUI2 = 0.85, and HUI3 = 0.78. Mean health profile scores were as follows: PORPUS-P = 71.7, PCI sexual, urinary, and bowel function = 23.7, 79.1, and 84.6, respectively (0 = worst, 100 = best), and FACT-P = 125.1 (0 = worst, 156 = best). In multiple regression analyses, comorbidity and PCI urinary, sexual, and bowel function were significant predictors of other QOL measures. With all variables, 32-50 % of the variance in utilities was explained. CONCLUSIONS: Many variables affect global QOL of PC survivors; only prostate symptoms and comorbidity have independent effects. Our model allows estimation of the effects of multiple factors on utilities. These utilities for long-term outcomes of PC and its treatment are valuable for decision/cost-effectiveness models of PC treatment.

TÍTULO / TITLE: Case Report: Binding of a Clinically Relevant Human Leukocyte Antigen-DQalpha-Specific Antibody in a Kidney Graft Recipient is Inhibited by Donor-Type Human Leukocyte Antigen-DQbeta Chain.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Mikkelsen S; Korsholm T; Iburg A; Petersen MS; Moller BK
INSTITUCIÓN / INSTITUTION: - Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark. Electronic address: susanmikkelsen@live.dk.

RESUMEN / SUMMARY: - In this case report, we have found what may be an immunization with donor-specific human leukocyte antigen (HLA)-DQalpha in combination with recipient-specific HLA-DQbeta. A renal allograft recipient who did not comply with immunosuppressive therapy during pregnancy had graft failure 23 months posttransplantation with biopsy-proven humoral and cellular rejection. Sera were tested in a Luminex-based single-antigen bead assay. We compared Luminex reactivity with the degree of eplet mismatching between the recipient’s own HLA-DQ chains and the HLA-DQ chains bound to the Luminex beads. Eplet calculations were done with the HLAMatchmaker. HLA-DQ similarities were compared further by dissimilarity scoring in HistoCheck. We observed that Luminex beads with donor-type HLA-DQalpha and HLA-DQbeta bound less antibody than beads with donor-type HLA-DQalpha combined with recipient HLA-DQbeta. In HLAMatchmaker, we identified all eplet mismatches between donor and recipient HLA-DQ. Next, we counted how many of these eplets were represented on the various Luminex beads. We found that antibody binding to the bead increased with the number of such mismatches for HLA-DQalpha. Surprisingly, antibody binding decreased as the number of eplet mismatches for HLA-DQbeta increased, from a mean fluorescence intensity (MFI) value of 18,800 for no mismatched eplets to approximately 10,000 for 12 mismatched eplets. These findings were confirmed by comparing antibody binding with the structural dissimilarity score between the recipient HLA-DQ type and the HLA-DQ bound to the Luminex beads. In this patient, clinically relevant antibodies bound strongly to donor-like HLA-DQalpha chains when combined with recipient-like HLA-DQbeta. HLA-DQbeta chains more similar to those of the donor reduced the binding of donor-specific HLA-DQalpha antibody.

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TÍTULO / TITLE: - Androgen-responsive Serum Response Factor target genes regulate prostate cancer cell migration.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Verone AR; Duncan K; Godoy A; Yadav N; Bakin A; Koochekpour S; Jin JP; Heemers HV

INSTITUCIÓN / INSTITUTION: - Department of Urology.
RESUMEN / SUMMARY: - Progression of prostate cancer (CaP) relies on androgen receptor (AR) signaling, but AR-dependent events that underlie the lethal phenotype remain unknown. Recently, an indirect mechanism of
androgen action in which effects of AR on CaP cells are mediated by Serum Response Factor (SRF) has been identified. This is the first mode of androgen action to be associated with aggressive CaP and disease recurrence. The manner in which androgen-responsive SRF activity controls aggressive CaP cell behavior is unknown. Here, the contribution of two representative SRF effector genes that are underexpressed, calponin 2 (CNN2), or overexpressed, sidekick-homolog 1 (SDK1), in clinical CaP specimens is studied. AR- and SRF-dependency of CNN2 and SDK1 expression was verified using synthetic and natural androgens, antiandrogens, and small interfering RNAs targeting AR or SRF, and evaluating the kinetics of androgen induction and SRF binding to endogenously and exogenously expressed regulatory gene regions in AR-positive CaP model systems that mimic the transition from androgen-stimulated to castration-recurrent disease. Small interfering RNA-mediated deregulation of CNN2 or SDK1 expression did not affect CaP cell proliferation or apoptosis but had marked effects on CaP cell morphology and actin cytoskeleton organization. Loss of CNN2 induced cellular protrusions and increased CaP cell migration, whereas silencing of SDK1 led to cell rounding and blunted CaP cell migration. Changes in cell migration did not involve epithelial-mesenchymal transition but correlated with altered beta1-integrin expression. Taken together, individual androgen-responsive SRF target genes affect CaP cell behavior by modulating cell migration, which may have implications for therapeutic intervention downstream of AR and SRF.

[322]
**TÍTULO / TITLE:** Re: cancer stem-like cells contribute to Cisplatin resistance and progression in bladder cancer.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2012.12.037
**AUTORES / AUTHORS:** Atala A

[323]
**TÍTULO / TITLE:** Re: Both Osteopontin-c and Osteopontin-b Splicing Isoforms Exert Pro-Tumorigenic Roles in Prostate Cancer Cells.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.02.106
**AUTORES / AUTHORS:** Atala A
[324] **Título / Title:** MicroRNA-101 suppresses motility of bladder cancer cells by targeting c-Met.

**Resumen / Summary:**

[Título / Title:](#) MicroRNAs (miRNAs) are small non-coding RNAs that play regulatory roles by repressing translation or cleaving RNA transcripts. Here, we report that the expression of microRNA-101 (miR-101) is down-regulated in human bladder cancer tissue versus normal adjacent tissue. To better characterize the role of miR-101 in bladder cancer, we conducted a gain-of-function analysis by transfecting the bladder cancer cell line T24 with chemically synthesized miR-101 mimics. We found that miR-101 directly targets c-Met via its 3'-UTR. Specifically, forced expression of miR-101 decreased c-Met expression at both mRNA and protein levels, consequently inhibiting T24 cell migration and invasion in a c-Met-dependent manner. In conclusion, we have shown miR-101 to be a novel suppressor of T24 cell migration and invasion through its negative regulation of c-Met.

[325] **Título / Title:** Contributors To HMGB1 Release By Urothelial Carcinoma Cells In Response To BCG.

**Resumen / Summary:**

[Título / Title:](#) INTRODUCTION: Prior work by our group has shown that HMGB1 release by urothelial carcinoma (UC) cells occurs as a consequence of BCG induced non-apoptotic cell death. Additional studies have demonstrated that HMGB1 release in response to BCG is required for the in vivo tumor response to BCG. This study evaluated the steps required for HMGB1 release by human UC cells in response to BCG exposure. MATERIALS
AND METHODS: Two human UC cells lines T24 and 253 were employed. HMGB1 concentrations in cell culture supernatant, with and without BCG treatment, served as the principal end point to assess the role of potentially involved variables. Specific techniques were utilized to determine the role of alpha5beta1 antigen receptor crosslinking, Toll Like Receptor signaling, BCG adherence, BCG internalization, BCG viability, iNOS expression/NO production, and p21 expression. RESULTS: Crosslinking of alpha5beta1 integrin, or signaling through TLR2/4, did not contribute to HMGB1 release. Optimal HMGB1 release required both BCG adherence and internalization. BCG viability was correlated with the magnitude of the HMGB1 release. Inhibition of oxidative stress and p21 expression in response to BCG reduced the magnitude of HMGB1 release. CONCLUSIONS: BCG induced non-apoptotic cell death and HMGB1 release occurs as a consequence of a complex multi-step process. An understanding of the steps and mechanisms involved in BCG induced HMGB1 release affords an opportunity for targeted strategies to improve BCG treatment efficacy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2012.12.038
AUTORES / AUTHORS: - Anthony A

[327] TÍTULO / TITLE: - Coffee consumption and the risk of prostate cancer: the Ohsaki Cohort Study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.238
AUTORES / AUTHORS: - Li Q; Kakizaki M; Sugawara Y; Tomata Y; Watanabe T; Nishino Y; Tsuji I
INSTITUCIÓN / INSTITUTION: - 1] Division of Epidemiology, Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan [2] Department of Epidemiology and Health Statistics, School of Public Health, Xi’an Jiaotong University College of Medicine, Xi’an, China.
RESUMEN / SUMMARY: - Background: Epidemiological evidence regarding the effect of coffee on the incidence of prostate cancer is inconsistent. We aimed to investigate coffee consumption and the risk of prostate cancer risk in a general
Japanese population.

Methods: We conducted a prospective cohort study in Ohsaki city, Japan, where 18,853 men aged 40-79 years participated in a baseline survey. Coffee consumption was assessed via a validated self-administered questionnaire. During 11 years of follow-up (from January 1, 1995 to December 31, 2005), 318 incident cases of prostate cancer were detected. The Cox proportional hazards regression model was used to calculate the hazard ratios (HRs) and 95% confidence interval (CIs).

Results: There was a significant inverse association between coffee consumption and the incidence risk of prostate cancer. Compared with those who did not drink coffee, the multivariate adjusted HRs were 0.81 (95% CI: 0.61 - 1.07), 0.73 (95% CI: 0.53 - 1.00), and 0.63 (95% CI: 0.39 - 1.00) for those who drank coffee occasionally, 1-2 cups per day, and >/=3 cups per day, respectively, with P for trend of 0.02.

Conclusion: This prospective finding from a Japanese population adds evidence that coffee intake is inversely associated with the incidence of prostate cancer.


[328]

TÍTULO / TITLE: - CXC chemokine receptor 4 is essential for maintenance of renal cell carcinoma-initiating cells and predicts metastasis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●● Enlace al texto completo (gratuito o de pago) 1002/stem.1407

AUTORES / AUTHORS: - Gassenmaier M; Chen D; Buchner A; Henkel L; Schiemann M; Mack B; Schendel DJ; Zimmermann W; Pohla H

INSTITUCIÓN / INSTITUTION: - Tumor Immunology Laboratory, LIFE Center, Ludwig-Maximilians-Universitat, Munich, Germany.

RESUMEN / SUMMARY: - In many solid tumors, cancer stem cells (CSC) represent a small cell population with tumor-initiating, self-renewal and differentiation potential, which can be identified by surface protein markers. No generally applicable markers are yet known for renal cell carcinoma (RCC). Two RCC cell lines (RCC-26, RCC-53) were found to differ widely in their capacity to form spheres in vitro and to establish tumors in mice, potentially reflecting differences in CSC content. A subpopulation expressing the CXC chemokine receptor 4 (CXCR4) was present only in the more tumorigenic cell line RCC-53. When grown as spheres, most of the RCC-53 cells were CXCR4-positive, expressed stem cell-associated transcription factor genes at elevated levels and were more resistant towards the tyrosine kinase inhibitors sunitinib, sorafenib and pazopanib. Sorted CXCR4-positive cells exhibited greater capacity for sphere formation and tumor growth-inducing potential in vivo than CXCR4-negative cells. Significantly, higher CXCR4 mRNA levels in primary RCC tumors from patients with localized but not disseminated disease predicted...
longer survival. Downregulation of CXCR4 expression by siRNA or pharmacological inhibition by AMD3100 compromised tumor sphere formation, viability of CXCR4-positive cells and increased their responsiveness towards tyrosine kinase inhibitors. In conclusion, CXCR4 identifies a subpopulation of tumor-initiating cells in RCC cell lines and plays a role in their maintenance. The relative insensitivity of such cells to tyrosine kinase inhibitors might contribute to the development of therapy resistance in RCC patients. Future therapies therefore could combine blockade of the CXCR4 signaling pathway with standard therapies for more effective treatments of metastatic RCC.

[329]

TITULO / TITLE: Consideration of comorbidity in risk stratification prior to prostate biopsy.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Liss MA; Billimek J; Osann K; Cho J; Moskowitz R; Kaplan A; Szabo RJ; Kaplan SH; Greenfield S; Dash A
INSTITUCIÓN / INSTITUTION: Department of Urology, University of California at Irvine, Irvine, California; Department of Urology, Long Beach Veterans Affairs Medical Center, Long Beach, California.
RESUMEN / SUMMARY: BACKGROUND: Previously, the patient-reported Total Illness Burden Index for Prostate Cancer (TIBI-CaP) questionnaire and/or the physician-reported Charlson Comorbidity Index (CCI) have provided assessments of competing comorbidity during treatment decisions for patients with prostate cancer. In the current study, the authors used these assessments to determine comorbidity and prognosis before prostate biopsy and the subsequent diagnosis of prostate cancer to identify those patients least likely to benefit from treatment. METHODS: A prospective observational cohort study was performed of 104 participants aged 64.0 years +/- 6.5 years from 3 institutions representing different health care delivery systems. Patients were identified before undergoing transrectal ultrasound-guided prostate biopsy and followed for a median of 28 months. Associations between the comorbidity scores and nonelective hospital admissions were investigated using logistic regression and Cox proportional hazards models. RESULTS: Among the 104 patients who underwent prostate biopsy, 2 died during the follow-up period. The overall hospital admission rate was 20% (21 of 104 patients). Higher scores on both the TIBI-CaP (>/= 9) and CCI (>/= 3) were found to be significantly associated with an increased odds for hospital admission (odds ratio, 11.3 [95% confidence interval (95% CI), 2.4-53.6] and OR, 5.7 [95% CI, 1.4-22.4]) and hazards ratios (HRs) for time to hospital admission (HR, 3.8 [95% CI, 1.3-11.2] and HR, 3.2 [95% CI, 1.1-9.1]), respectively. CONCLUSIONS: TIBI-CaP and
CCI scores were found to successfully predict which patients were at high risk for nonelective hospital admission. These patients are likely to have poorer health and a potentially shortened lifespan. Therefore, comorbidity analysis using these tools may help to identify those patients who are least likely to benefit from prostate cancer therapy and should avoid prostate biopsy. Cancer 2013. © 2013 American Cancer Society.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

 Enlace al texto completo (gratuito o de pago)

AUTORES / AUTHORS: - Kim SM; Kim HW; Lee EK; Park SK; Han DJ; Kim SB

INSTITUCIÓN / INSTITUTION: - 1 Division of Nephrology, Department of Internal Medicine, Jeju National University Hospital, Jeju, South Korea. 2 Division of Nephrology, Department of Internal Medicine, Dankook University Hospital, Cheonansi, South Korea. 3 Division of Nephrology, Department of Internal Medicine, Asan Medical Center, Seoul, South Korea. 4 Department of General Surgery, Asan Medical Center, Seoul, South Korea. 5 Address correspondence to: Soon Bae Kim, M.D., Division of Nephrology, Department of Internal Medicine, Asan Medical Center, 388-1, Pungnap-2 dong, Songpa-gu, Seoul 138-736, South Korea.

RESUMEN / SUMMARY: - BACKGROUND: Some guidelines recommend a liver biopsy to all anti-hepatitis C virus (HCV) antibody-positive kidney transplant (KT) recipients. However, in the case of HCV RNA-negative KT recipients, the benefit of a liver biopsy is unclear. We examined the usefulness of a liver biopsy for anti-HCV antibody-positive and HCV RNA-negative patients by analyzing the hepatic histologic findings and clinical outcomes. METHODS: A total of 30 anti-HCV antibody-positive patients who underwent liver biopsy before KT at Asan Medical Center were retrospectively recruited. The patients were divided into two groups based on HCV RNA positivity: 17 patients were positive and 13 patients were negative. Histologic evidence of hepatic inflammation and fibrosis was assessed using the METAVIR score, and clinical outcomes, including mortality, graft loss, and progression of liver disease, were compared. RESULTS: The mean histologic activity scores for inflammation and fibrosis for the HCV RNA-positive and HCV RNA-negative groups were significantly different (inflammation score 1.11+/−0.85 vs. 0.46+/−0.51; P=0.01 and fibrosis score 1.05+/−1.24 vs. 0.15+/−0.37; P=0.01, respectively). The overall rates of mortality and graft loss were not significantly different between the two groups. Progression of liver disease was noted in the HCV RNA-positive group only. CONCLUSION: The HCV RNA-negative group showed no evidence of liver disease progression. Neither did they show any histologic evidence of liver inflammation and fibrosis before KT. Therefore, it appears that liver biopsy is not necessary in anti-HCV antibody-positive and HCV RNA-negative KT recipients.

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TÍTULO / TITLE: - Cooperation of histone deacetylase inhibitors SAHA and valproic acid in promoting sodium/iodide symporter expression and function in rat Leydig testicular carcinoma cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1007/s12020-013-9972-4

AUTORES / AUTHORS: - Maggisano V; Puppin C; Celano M; D’Agostino M; Sponziello M; Micali S; Navarra M; Damante G; Filetti S; Russo D

INSTITUCIÓN / INSTITUTION: - Department of Health Sciences, University of Catanzaro ‘Magna Graecia’, Viale Europa, loc. Germaneto, 88100, Catanzaro, Italy.

RESUMEN / SUMMARY: - The presence of the sodium/iodide symporter (NIS) is the prerequisite for the use of the radioiodine in the treatment of thyroid cancer. Thus, stimulators of NIS expression and function are currently investigated in cellular models of various human malignancies, also including extrathyroid cancers. In this study, we analyzed the effects of the histone deacetylase inhibitors (HDACi), suberoylanilide hydroxamic acid (SAHA) and valproic acid (VPA), on NIS expression and function in rat Leydig testicular carcinoma cells (LC540). LC540 cells were exposed to SAHA 3 μM and VPA 3 mM (alone and in combination), and cell viability evaluated by MTT assay and cell counting, NIS mRNA and protein levels by using, respectively, real-time RT-PCR and western blotting. NIS function was evaluated by iodide uptake assay. We found that both HDACi were able to stimulate the transcription of NIS gene, but not its protein expression, while the association of SAHA and VPA increased both NIS transcript and protein levels, resulting in significant sixfold enhancement of radioiodine uptake capacity of LC540 cells. These data demonstrate the presence of an epigenetic control of NIS expression in Leydig tumor cells, suggesting the possibility to use the combination of these two HDACi for a radioiodine-based treatment of these malignancies.

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[333]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 3892/ijo.2013.1877

AUTORES / AUTHORS: - Zhang N; Wu P; Shayiremu D; Wu L; Shan H; Ye L; Zhao X; Cai J; Jiang WG; Gong K; Yang Y

INSTITUCIÓN / INSTITUTION: - Department of Urology, Beijing Chaoyang Hospital, Capital Medical University, Beijing 100020, PR China.

RESUMEN / SUMMARY: - Vascular endothelial growth inhibitor (VEGI) has been associated with tumor-related vasculature in certain malignancies. However, its implication in renal cell carcinoma (RCC), an angiogenesis-dependent tumor,
remains unknown. In the present study, we investigated the role played by VEGI in RCC. The expression of VEGI was examined in human renal tissue and RCC cell lines using immunohistochemical staining and RT-PCR, respectively. The biological impact of modifying the expression of VEGI in RCC cells was evaluated using in vitro and in vivo models. We show that VEGI mRNA is expressed in a wide variety of human RCC cell lines, all of normal renal and most of RCC tissue specimens. VEGI protein expression was observed in normal renal tubular epithelial cells, but was decreased or absent in RCC specimens, particularly in tumors with high grade. Moreover, forced expression of VEGI led to an inhibition of vascular endothelial tube formation, decrease in the motility and adhesion of RCC cells in vitro. Interestingly, forced expression of VEGI had no bearing on growth, apoptosis and invasive capacity of RCC cells. However, tumor growth was reduced in xenograft models. Immunohistochemical staining showed that microvessel density decreased in VEGI forced expression xenograft tumor samples. Taken together, our findings showed that the expression of VEGI is decreased in RCC, particularly in tumors with higher grade. Together with its inhibitory effect on cellular motility, adhesion, vascular endothelial tube formation and tumor growth in vivo, this suggests that VEGI functions mainly through inhibition of angiogenesis and is a negative regulator of aggressiveness during the development and progression of RCC.

[334]

TÍTULO / TITLE: - Re: posterior urethral complications of the treatment of prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Morey AF

[335]

TÍTULO / TITLE: - Sub-nanomolar Detection of Prostate-Specific Membrane Antigen in Synthetic Urine by Synergistic, Dual-Ligand Phage.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Mohan K; Donavan KC; Arter JA; Penner RM; Weiss GA
INSTITUCIÓN / INSTITUTION: - Departments of section signChemistry, double daggerMolecular Biology & Biochemistry, and daggerChemical Engineering &
RESUMEN / SUMMARY: - The sensitive detection of cancer biomarkers in urine could revolutionize cancer diagnosis and treatment. Such detectors must be inexpensive, easy to interpret, and sensitive. This report describes a bioaffinity matrix of viruses integrated into PEDOT films for electrochemical sensing of prostate-specific membrane antigen (PSMA), a prostate cancer biomarker. High sensitivity to PSMA resulted from synergistic action by two different ligands to PSMA on the same phage particle. One ligand was genetically encoded, and the secondary recognition ligand was chemically synthesized to wrap around the phage. The dual ligands result in a bidentate binder with high-copy, dense ligand display for enhanced PSMA detection through a chelate-based avidity effect. Biosensing with virus-PEDOT films provides a 100 pM limit of detection for PSMA in synthetic urine without requiring enzymatic or other amplification.

TÍTULO / TITLE: - Efficacy and safety of photodynamic therapy in recurrent high-grade non-muscle-invasive bladder cancer refractory or intolerant to bacille Calmette-Guerin immunotherapy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Lee JY; Diaz RR; Cho KS; Lim MS; Chung JS; Kim WT; Ham WS; Choi YD
INSTITUCIÓN / INSTITUTION: - Department of Urology, Severance Hospital, Urological Science Institute, Yonsei University College of Medicine, Seoul, Korea.
RESUMEN / SUMMARY: - PURPOSE: To evaluate Photodynamic therapy (PDT) effectiveness using Radachlorin® in patients with high-grade non-muscle-invasive bladder cancer (NMIBC) refractory or intolerant to bacille Calmette-Guerin (BCG) therapy, for which radical cystectomy was refused. MATERIALS AND METHODS: Between July 2009 and December 2011, PDT was performed in 34 patients (22 men/12 women). Radachlorin (0.5-0.6 mg/kg) was intravenously injected 2-3 hours before PDT. After complete transurethral resection, a diffuser using a 22 Fr. cystoscope was placed into the bladder for irradiation with a 662 nm laser. The output beam power was adjusted to 1.8 W, light dose was 15 J/cm2, and PDT was performed for 16-30 minutes. Recurrence after PDT was followed by regular cystoscopy at 1, 2, and 3-months, and thereafter at 3-month intervals for up to 2.8 years. Efficacy was assessed by cystoscopy, cytology, and histology, and was defined as the number of patients who were tumor-free after initial PDT. RESULTS: Mean
patient age was 62.94+/−8.71 years. Average follow-up was 26.74+/−6.34 months (median 28.12 months). In primary efficacy outcome, recurrence-free rates were 90.9% at 12-months, 64.4% at 24 months, and 60.1% at 30 months. In secondary efficacy outcome, there were no statistical differences in mass size, carcinoma in situ number of previous BCG or transurethral resection of bladder therapies and multiplicity (P>0.05 in all comparisons), using Kaplan-Meier analyses. No evidence of severe adverse effects was detected after PDT.

CONCLUSIONS: PDT with Radachlorin is a safe and effective treatment for NMIBC refractory or intolerant to BCG therapy in selected patients.

[337]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1016/S1470-2045(13)70162-1

AUTORES / AUTHORS: - Ko YJ; Canil CM; Mukherjee SD; Winquist E; Elser C; Eisen A; Reaume MN; Zhang L; Sridhar SS

INSTITUCIÓN / INSTITUTION: - Sunnybrook Odette Cancer Centre, Toronto, ON, Canada.

RESUMEN / SUMMARY: - BACKGROUND: No standard treatment exists for patients with platinum-refractory urothelial cancer. Taxanes and vinflunine are commonly used, but response is less than 20% with no survival benefit. In this phase 2 study, we assessed efficacy and tolerability of nanoparticle albumin-bound (nab) paclitaxel in platinum-refractory urothelial cancer. METHODS: We did an open-label, single-group, two-stage study at five centres in Canada. We enrolled patients aged at least 18 years with histologically confirmed, locally advanced, or metastatic measurable urothelial cancer, with documented progression on or within 12 months of treatment with one previous platinum-containing regimen. Patients received nab-paclitaxel at 260 mg/m2 intravenously every 3 weeks. Treatment continued until disease progression or occurrence of unacceptable toxic effects. The primary endpoint was objective tumour response, defined by a complete response (CR) or partial response (PR) according to Response Evaluation Criteria in Solid Tumors (version 1.0) criteria. Tumour response and safety were assessed in all patients who received at least one cycle of nab-paclitaxel. This study is registered with ClinicalTrials.gov, number NCT00683059. FINDINGS: We enrolled 48 patients between Oct 16, 2008, and June 23, 2010. Patients received a median of six cycles (range one to 15). 47 patients were evaluable; one (2.1%) had a CR and
12 (25.5%) had PRs, resulting in an overall response of 27.7% (95% CI 17.3-44.4). The most frequently recorded adverse events of any grade were fatigue (38 of 48; 79%), pain (37 of 48; 77%), alopecia (34 of 48; 71%), and neuropathy (30 of 48; 77%). The most frequently recorded adverse events of grade 3 or higher were pain (11 of 48; 23%), fatigue (five of 48; 23%), hypertension (three of 48; 6%), neuropathy (three of 48, 6%), and joint stiffness or pain (two of 48; 4%). INTERPRETATION: Nab-paclitaxel was well tolerated in this population of patients with pretreated advanced urothelial cancer with an encouraging tumour response. These results warrant further study of nab-paclitaxel in second-line treatment of urothelial cancer. FUNDING: Abraxis Bioscience, Celgene.
than 70 years with a low score of TIDCs. None of 20 patients with a low score of TAMs progressed. These data indicate that the presence of mature TIDCs and possibly TAMs may help risk-stratify patients at the time of first diagnosis of non-muscle-invasive bladder cancer and may be useful in tailoring follow-up and treatment strategies.

[339]

TÍTULO / TITLE: - Cigarette smoke induces nuclear translocation of heme oxygenase 1 (HO-1) in prostate cancer cells: nuclear HO-1 promotes vascular endothelial growth factor secretion.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Birrane G; Li H; Yang S; Tachado SD; Seng S

INSTITUCIÓN / INSTITUTION: - Division of Experimental Medicine, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, USA.

RESUMEN / SUMMARY: - Prostate cancer is the second leading cause of male cancer related death in the United States. Despite a number of evidence-based studies which strongly suggest an association between cigarette smoking and prostate cancer, the underlying biological mechanism is largely unknown. Heme oxygenase 1 (HO-1) has been implicated in maintaining cellular homeostasis, but also in tumor angiogenesis. Nuclear HO-1 protein expression has been observed in various types of tumors including prostate cancer. These studies, however, were reported as clinical and pathological observations, and failed to investigate nuclear HO-1 at the molecular level in cancer. The present study explores the relationship between cigarette smoke and nuclear HO-1-modulated promotion of vascular endothelial growth factor (VEGF) secretion. We have demonstrated that cigarette smoke medium (SM)-induced HO-1 mRNA expression and upregulated HO-1 protein levels in the prostate cancer cell lines DU145 and PC3. We also observed that SM significantly induced nuclear expression of HO-1, and enhanced secretion of VEGF in cells. Nuclear-directed expression of HO-1 activated the transcriptional activity of VEGF and promoted VEGF secretion in prostate cancer cells. This study provides new insights into the molecular mechanism by which cigarette smoke-induced nuclear translocation of HO-1 promotes VEGF secretion in prostate cancer cells. Nuclear HO-1 may, therefore, constitute an attractive therapeutic target to inhibit angiogenesis and the progression of prostate cancer.

[340]
Intravesical gemcitabine for high-risk non-muscle-invasive bladder cancer after bacillus Calmette-Guerin treatment failure.

**RESUMEN / SUMMARY:** To report our experience with intravesical gemcitabine for bladder cancer after failure of treatment with bacillus Calmette-Guerin (BCG). MATERIALS AND METHODS: A retrospective review of patients treated with intravesical gemcitabine after BCG failure at our cancer center. Progression-free survival (PFS), recurrence-free survival (RFS) and cancer-specific survival (CSS) were estimated using the cumulative incidence function, considering death from other causes as a competing risk. Comparisons were made using Gray’s test. Overall survival (OS) was estimated using Kaplan-Meier methods and differences were compared with the log-rank test. RESULTS: Of 69 patients treated with intravesical gemcitabine, 37 had BCG-refractory disease. Median follow-up in progression-free patients was 3.3 years. PFS and CSS were similar among patients with BCG-refractory disease and patients with other types of BCG failures. OS was lower for patients with BCG-refractory disease (58% vs. 71%), but not statistically significant (p = 0.096). Twenty-seven patients experienced a complete response (CR). PFS, CSS, and OS did not differ significantly between patients with CR and those without. Twenty patients had subsequent cystectomy. Patients with CR had delayed time to cystectomy and no MIBC at cystectomy. There were no serious adverse events, and only a minority of patients had to discontinue treatment due to adverse events. CONCLUSIONS: In our experience intravesical gemcitabine should be considered after BCG failure in patients with bladder cancer who refuse radical cystectomy or are unfit for major surgery.

RESUMEN / SUMMARY: - Analyze the expression of the serine protease HtrA1 in human bladder tissue and urine in order to point out its possible association with the presence of urothelial bladder cancer. Bladder tissue and urine specimens from cancer patients with different tumour grades and stages (n=68) and from individuals with cystitis (n=16) were collected along with biopsy specimens and urine from healthy individuals (n=68). For the first time, we demonstrated by immunohistochemistry that HtrA1 protein is produced by bladder urothelium in both physiological and inflammatory conditions, whereas it is not detectable in urothelial cancer cells regardless of tumour grade and stage. A different HtrA1 expression between normal-looking and neoplastic bladder tissue, despite similar HtrA1 mRNA levels, was also found by western blotting, which disclosed the presence of two forms of HtrA1, a native form of ~50 kDa and an autocatalytic form of ~38 kDa. Our investigations documented the presence of the two forms of HtrA1 also in urine. The ~38 kDa form was significantly down-regulated in neoplastic tissue, whereas significantly higher amounts of both HtrA1 forms were found in urine from cancer patients compared with both healthy subjects and patients with cystitis. Our findings suggest that HtrA1 is a downexpressed molecule since an early stage of bladder urothelial carcinoma development and that urinary HtrA1 protein may be considered, if successfully validated, as an early and highly sensitive and specific biomarker for this neoplasia (the sensitivity and specificity of HtrA1 are 92.65% and 95.59%, respectively). © 2013 Wiley Periodicals, Inc.

AUTORES / AUTHORS: - Lorenzi T; Lorenzi M; Altobelli E; Marzioni D; Mensa E; Quaranta A; Paolinelli F; Morroni M; Mazzucchelli R; De Luca A; Procopio AD; Baldi A; Muzzonigro G; Montironi R; Castellucci M

INSTITUCIÓN / INSTITUTION: - Department of Experimental and Clinical Medicine, Universita Politecnica delle Marche, Via Tronto 10/a, 60020 Ancona, Italy.

MINIREVIEW: - The molecular and genomic basis for prostate cancer health disparities.

RESUMEN / SUMMARY: - Our aim was to analyze the expression of the serine protease HtrA1 in human bladder tissue and urine in order to point out its possible association with the presence of urothelial bladder cancer. Bladder tissue and urine specimens from cancer patients with different tumour grades and stages (n=68) and from individuals with cystitis (n=16) were collected along with biopsy specimens and urine from healthy individuals (n=68). For the first time, we demonstrated by immunohistochemistry that HtrA1 protein is produced by bladder urothelium in both physiological and inflammatory conditions, whereas it is not detectable in urothelial cancer cells regardless of tumour grade and stage. A different HtrA1 expression between normal-looking and neoplastic bladder tissue, despite similar HtrA1 mRNA levels, was also found by western blotting, which disclosed the presence of two forms of HtrA1, a native form of ~50 kDa and an autocatalytic form of ~38 kDa. Our investigations documented the presence of the two forms of HtrA1 also in urine. The ~38 kDa form was significantly down-regulated in neoplastic tissue, whereas significantly higher amounts of both HtrA1 forms were found in urine from cancer patients compared with both healthy subjects and patients with cystitis. Our findings suggest that HtrA1 is a downexpressed molecule since an early stage of bladder urothelial carcinoma development and that urinary HtrA1 protein may be considered, if successfully validated, as an early and highly sensitive and specific biomarker for this neoplasia (the sensitivity and specificity of HtrA1 are 92.65% and 95.59%, respectively). © 2013 Wiley Periodicals, Inc.
RESUMEN / SUMMARY: - Despite more aggressive screening across all demographics and gradual declines in mortality related to prostate cancer (PCa) in the United States, race disparities persist. For African American men (AAM), PCa is more often an aggressive disease showing increased metastases and greater PCa-related mortality compared with European American men. The earliest research points to how distinctions are likely the result of a combination of factors, including ancestry genetics and lifestyle variables. More recent research considers that cancer, although influenced by external forces, is ultimately a disease primarily driven by aberrations observed in the molecular genetics of the tumor. Research studying PCa predominantly from European American men shows that indolent and advanced or metastatic prostate tumors have distinguishing molecular genomic make-ups. Early yet increasing evidence suggests that clinically distinct PCa from AAM also display molecular distinctions. It is reasonable to predict that further study will reveal molecular subtypes and various frequencies for PCa subtypes among diverse patient groups, thereby providing insight as to the genomic lesions and gene signatures that are functionally implicated in carcinogenesis or aggressive PCa in AAM. That knowledge will prove useful in developing strategies to predict who will develop advanced PCa among AAM and will provide the rationale to develop effective individualized treatment strategies to overcome disparities.

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TÍTULO / TITLE: - Androgen receptor promotes the migration and invasion of upper urinary tract urothelial carcinoma cells through the upregulation of MMP-9 and COX-2.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Chen CC; Hsieh TF; Chang CH; Ma WL; Hung XF; Tsai YR; Lin MH; Zhang C; Chang C; Shyr CR

INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Surgery, Buddhist Tzu Chi General Hospital, Taichung Branch, Taichung 427, Taiwan, R.O.C.

RESUMEN / SUMMARY: - Dysregulated androgen receptor (AR) signaling is implicated in several types of tumor, including carcinomas of the prostate, breast, liver and bladder. However, the contribution of AR to the progression of upper urinary tract urothelial carcinomas (UUTUC) has not been fully investigated. In the present study, we demonstrated that the AR is involved in the metastasis and invasiveness of UUTUC cells. We investigated the role of
the AR in UUTUC by using UUTUC-derived BFTC 909 cells. The overexpression of AR promotes the migration and invasion of BFTC 909 cells. Expression of migration/invasion-related genes was increased in BFTC 909 cells overexpressing AR determined by qPCR and western blot analyses. The results showed that AR-enhanced migration and invasion of UUTUC cells are linked to the upregulation of the matrix-degrading enzyme MMP-9 and cyclooxygenase (COX)-2. Subsequently, the blocking of MMP-9 and COX-2 signaling by inhibitors suppressed AR-enhanced cell migration and invasion. The results of the present study provide evidence for the first time of the role of AR in the motility and invasion of UUT cancer cells and support the hypothesis that the AR may play a critical role in the establishment of the invasive phenotype in urothelial neoplasia of UUT. Thus, the AR may also serve as a novel biomarker and potential therapeutic target for UUT cancer.

[345]

TÍTULO / TITLE: - Endoscopic Vascular Targeted Photodynamic Therapy with the Photosensitizer TOOKAD® Soluble (WST11) for Benign Prostatic Hyperplasia in the Pre-Clinical Dog Model.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Chevalier S; Cury FL; Scarlata E; El-Zayat E; Hamel L; Rocha J; Zouanat F; Moussa S; Scherz A; Elhilali M; Anidjar M
INSTITUCIÓN / INSTITUTION: - Urologic Oncology Research Group, McGill University Health Center (MUHC)-Research Institute (RI), 1650 Cedar Avenue, Montreal, QC, Canada, H3G 1B4. Electronic address: simone.chevalier@mcgill.ca.

RESUMEN / SUMMARY: - PURPOSE: Vascular Targeted Photodynamic (VTP) therapy with TOOKAD®Soluble is in phase III clinical trials through an interstitial transperineal approach for focal therapy of prostate cancer. Herein we investigated the safety and efficacy of the endourethral route in the context of Benign Prostatic Hyperplasia (BPH) in the dog model. MATERIALS AND METHODS: An optical laser fiber was positioned in the prostatic urethra of 34 dogs, including 4 controls, and connected to a 753nm diode laser at a fluence of 200mW/cm² delivering 200-300J. TOOKAD®Soluble (5-15mg/Kg) was infused i.v. in two modes: continuous, starting 5-15min prior and during illumination or a bolus 5-10min before. Prostate ultrasound, cystourethrography, urodynamics and histopathology were performed. Follow-up ranged from 1-week to 1-year. RESULTS: Endourethral TOOKAD®Soluble-VTP was uneventful in all but one dog experiencing urinary retention but reached the 1-week endpoint. All prostates except controls presented hemorrhagic lesions. They consisted of two
levels of concentric alterations: peri-urethral necrosis with destruction of the endothelial layer and adjacent inflammation/atrophy with normal blood vessels. Prostatic urethral width increased as early as 6 weeks post-treatment while prostatic volume decreased, reaching 25% by 18-26 weeks. A parallel decrease in urethral pressures was demonstrated at 6 weeks and lasted up to 1 year.

CONCLUSIONS: We confirmed the vascular effect of endourethral TOOKAD®Soluble-VTP and showed for the first time that resulting peri-urethral necrosis lead to a significant and sustained widening of the prostatic urethra, accompanied by long-term improvement of urodynamic parameters. These findings support future clinical applications of this minimally invasive approach for BPH treatment.

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[346]

**TITULO / TITLE:** Spondin-2, a secreted extracellular matrix protein, is a novel diagnostic biomarker for prostate cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Lucarelli G; Rutigliano M; Bettocchi C; Palazzo S; Vavallo A; Galleggiante V; Trabucco S; Di Clemente D; Selvaggi FP; Battaglia M; Ditonno P

**INSTITUCIÓN / INSTITUTION:** Department of Emergency and Organ Transplantation - Urology, Andrology and Kidney Transplantation Unit, University of Bari, Bari, Italy. Electronic address: giuseppe.lucarelli@inwind.it.

**RESUMEN / SUMMARY:** PURPOSE: Spondin-2 (SPON2) belongs to the F-spondin family of secreted extracellular matrix proteins and has been found to be deregulated in some tumors, including prostate cancer (PCa). In the present prospective study, we assessed the role of serum SPON2 as a biomarker for PCa diagnosis, as well as any association between SPON2 levels and clinical-pathological features. In addition, we compared the diagnostic performance of this biomarker to those of serum sarcosine, %free-PSA and total PSA.

**PATIENTS AND METHODS:** SPON2 was measured using a sandwich ELISA in serum samples from 286 PCa patients and 68 subjects with no evidence of malignancy (NEM), confirmed by 10-12 core ultrasound-guided prostate biopsies. Nonparametric statistical tests and receiver operating characteristics (ROC) analyses were performed to assess the diagnostic performance of SPON2 as compared to the other biomarkers

**RESULTS:** Median SPON2 serum levels were significantly higher in PCa patients than NEM patients (77.5 vs 23.6 ng/ml; p<0.0001). ROC analyses in subjects showed a higher predictive value of SPON2 (AUC=0.952) versus serum sarcosine (AUC=0.674), %free-PSA (AUC=0.806) and total PSA (AUC=0.561). Moreover, PCa patients with
low grade cancer showed higher median SPON2 levels (p=0.001). Spearman rank correlation confirmed a negative association with the Gleason score (rs=-0.29; p=0.0005). CONCLUSIONS: We found evidence that SPON2 levels were significantly higher in PCa patients than in healthy individuals. Moreover, this biomarker had a better diagnostic performance as compared to serum sarcosine, %fPSA and total PSA, and this higher accuracy was also present in a subset of patients with “normal” PSA values.

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[347] TÍTULO / TITLE: - Assessment of endothelial dysfunction by flow-mediated dilatation in men on long-term androgen deprivation therapy (ADT) for prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Gilbert SE; Tew GA; Bourke L; Winter EM; Rosario DJ
INSTITUCIÓN / INSTITUTION: - 1 Sheffield Hallam University;
RESUMEN / SUMMARY: - Androgen deprivation therapy (ADT) in men with prostate cancer has been linked to an increased incidence of cardiovascular events and mortality but the underpinning mechanisms are unclear. Endothelial dysfunction is considered a precursor for cardiovascular disease. Previous studies have reported variably on the association between ADT and endothelial function. This blinded case-control study examined endothelial function, using high-resolution ultrasound to measure flow-mediated dilatation (FMD) and glyceryl trinitrate (GTN)-mediated-dilatation in the brachial artery, in 20 men with prostate cancer (69 +/- 7 years) treated by ADT (median duration 22 months, range 6-133 months) and 20 men without prostate cancer (69 +/- 5 years) matched for age, physical activity, co-existent cardiovascular disease and body mass index. The magnitude of dilatation was calculated traditionally and allometrically-scaled, adjusted for baseline diameter. There were no differences between groups for resting vascular measures (mean +/- SD). FMD was lower in men on ADT than controls (3.9 +/- 2.1% versus 5.9 +/- 3.8% for "traditional", P = 0.047; 3.7 +/- 2.7% versus 6.0 +/- 2.7% for allometrically-scaled, P = 0.023). Response to GTN was similar in both groups (12.2 +/- 4.2% versus 14.8 +/- 5.7% for "traditional", P = 0.113; 12.3 +/- 4.6% versus 14.4 +/- 4.6% for allometrically-scaled, P = 0.163). The magnitude of difference in mean FMD between groups was marginally altered to 2.4% (95% CI 0.3 to 4.5) after adjustment for difference in body fat mass and concomitant cardiovascular medication, with the difference in FMD remaining significant (P = 0.029). There is evidence of endothelial dysfunction in men with prostate cancer on long-term ADT. Although a causal relationship is unproven, the findings are consistent
with observational reports of adverse cardiovascular outcomes associated with
long-term ADT for prostate cancer.

[348]
**TITULO / TITLE:** - MicroRNA-302ª sensitizes testicular embryonal carcinoma
cells to cisplatin-induced cell death.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** - Liu L; Lian J; Zhang H; Tian H; Liang M; Yin M; Sun F
**INSTITUCIÓN / INSTITUTION:** - Hefei National Laboratory for Physical Sciences at
Microscale and Department of Cell and Developmental Biology, School of Life
Sciences, University of Science and Technology of China, Hefei, Anhui,
230027, China.
**RESUMEN / SUMMARY:** - Cisplatin is a commonly used chemotherapeutic agent
for the treatment of several human malignancies, such as testicular germ cell
tumors (TGCT). The toxic effects persist and those that are present long after
chemotherapy affect the overall quality of life of patients. MicroRNAs (miRNAs)
play important roles in the responses of cancer cells to chemotherapy and have
been shown to modulate cell sensitivity to chemotherapeutic drugs. However,
the relationship between miRNA expression and cisplatin sensitivity of TGCT
has not been fully explored. In this study, the effects of miR-302ª on cisplatin
cytotoxicity in TGCT-derived cell line NTERA-2 (NT2) were evaluated. We
found that expression levels of miR-302ª were increased in cisplatin-treated
NT2 cells. Up-regulation of miR-302ª significantly increased the sensitivity of
NT2 cells to cisplatin by enhancing cisplatin-induced G2/M phase arrest and the
subsequent progression to apoptosis. MiR-302ª also increased the killing
effects of cisplatin by lowering the apoptotic threshold; the same result was also
observed in another TGCT-derived cell line, NCCIT. Furthermore, miR-302ª-
enhanced cisplatin sensitivity was partially mediated through the down-
regulation of p21 in NT2 cells. MiR-302ª induced apoptosis was further
enhanced by silencing of p53 in NT2 cells. p53 levels were inversely associated
with the expression of Oct4, Sox2 and Nanog in response to cisplatin. Thus,
targeting miR-302ª may offer new therapeutic interventions in TGCT. J. Cell.
Physiol. © 2013 Wiley Periodicals, Inc.

[349]
**TITULO / TITLE:** - Re: TP53INP1 as new therapeutic target in castration-resistant
prostate cancer.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.01.067

AUTORES / AUTHORS: - Atala A


Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.01.067

AUTORES / AUTHORS: - Liu Y; Gao F; Jiang H; Niu L; Bi Y; Young CY; Yuan H; Lou H

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Shandong University School of Medicine, Jinan 250012, China; Department of Natural Product Chemistry, Shandong University School of Pharmaceutical Sciences, Jinan 250012, China.

Enlace al texto completo (gratuito o de pago) 1016/j.canlet.2013.05.022

AUTORES / AUTHORS: - Liu Y; Gao F; Jiang H; Niu L; Bi Y; Young CY; Yuan H; Lou H


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Enlace al texto completo (gratuito o de pago) 1016/j.canlet.2013.05.022

AUTORES / AUTHORS: - Liu Y; Gao F; Jiang H; Niu L; Bi Y; Young CY; Yuan H; Lou H

RESUMEN / SUMMARY: - Induction of DNA damage and ATF3 by retigeric acid B, a novel topoisomerase II inhibitor, promotes apoptosis in prostate cancer cells.

RESUMEN / SUMMARY: - Retigeric acid B (RB) has been reported to exhibit its anti-tumor activity in vitro and in vivo. Here, we found that RB significantly inhibited activity of topoisomerase IIalpha (Topo IIalpha), leading to remarkable DNA damage in prostate cancer (PCa) cells as evidenced by a strong induction of gammaH2AX and DNA fragmentation. Activation of ATM and ATR sequentially led to induction of phospho-Chk1/2 and phospho-Cdc25 in response to RB. Blockade of ATM/ATR signaling resulted in the attenuation of RB-induced gammaH2AX, and partially rescued RB-mediated cell death. RB treatment also resulted in inactivation of DNA repair proteins such as phospho-BRCA1, impairment of HR, and NHEJ repair as indicated by DNA end-joining assays. Meanwhile, a stress-responsive gene activating transcription factor 3 (ATF3) was noted for its predominant expression in response to RB-induced DNA damage. Knockdown of ATF3 inhibited the RB-induced up-regulation of cell cycle- and apoptosis-related genes such as DR5, DDIT4, CDC25A, GADD45A, and partially blocked RB-mediated inhibition on cell proliferation and induction of apoptosis, suggesting the crucial involvement of ATF3 in this event. Microarray data displayed that RB caused changes of genes required for damaged-DNA binding and repair, as well as ATF3 and its target genes. Our data firstly demonstrated that RB was a novel DNA Topo II inhibitor and triggered cell death by inducing DNA damage and stress-response, suggesting a promising anticancer agent.

Enlace al Resumen / Link to its Summary

Enlace al Resumen / Link to its Summary
Angiotensin Receptor Blockers and Risk of Prostate Cancer Among United States Veterans.

RESUMEN / SUMMARY: To address concerns regarding increased risk of prostate cancer (PrCA) among angiotensin receptor blocker (ARB) users, we used national retrospective data from the Department of Veterans Affairs (VA) through the Veterans Affairs Informatics and Computing Infrastructure. We identified a total of 543,824 unique Veterans who were classified into either ARB treated or not-treated in 1:15 ratio. The two groups were balanced using inverse probability of treatment weights. A double-robust cox-proportional hazards model was used to estimate the hazard ratio for PrCA incidence. To evaluate for a potential Gleason score stage migration, we conducted weighted Cochrane-Armitage test. Post weighting, the rates of PrCA in treated and not-treated groups were 506 (1.5%) and 8,269 (1.6%), respectively; representing a hazard ratio of (0.91, p-value .049). There was no significant difference in Gleason scores between the two groups. We found a small, but statistically significant, reduction in the incidence of clinically detected PrCA among patients assigned to receive ARB with no countervailing effect on degree of differentiation (as indicated by Gleason score). Findings from this study support Food and Drug Administration’s recent conclusion that ARB use does not increase risk of incident PrCA.

Deregulated expression of urokinase and its inhibitor type 1 in prostate cancer cells: Role of epigenetic mechanisms.

RESUMEN / SUMMARY: To address concerns regarding increased risk of prostate cancer (PrCA) among angiotensin receptor blocker (ARB) users, we used national retrospective data from the Department of Veterans Affairs (VA) through the Veterans Affairs Informatics and Computing Infrastructure. We identified a total of 543,824 unique Veterans who were classified into either ARB treated or not-treated in 1:15 ratio. The two groups were balanced using inverse probability of treatment weights. A double-robust cox-proportional hazards model was used to estimate the hazard ratio for PrCA incidence. To evaluate for a potential Gleason score stage migration, we conducted weighted Cochrane-Armitage test. Post weighting, the rates of PrCA in treated and not-treated groups were 506 (1.5%) and 8,269 (1.6%), respectively; representing a hazard ratio of (0.91, p-value .049). There was no significant difference in Gleason scores between the two groups. We found a small, but statistically significant, reduction in the incidence of clinically detected PrCA among patients assigned to receive ARB with no countervailing effect on degree of differentiation (as indicated by Gleason score). Findings from this study support Food and Drug Administration’s recent conclusion that ARB use does not increase risk of incident PrCA.
Plasminogen activator inhibitor-1 (PAI-1) and urokinase-type plasminogen activator (uPA) play a crucial role in cancer progression. In the present study we examined the regulation of PAI-1 and uPA expressions in normal prostate epithelial cells (PrEC) and the prostate cancer cell lines LNCaP, DU-145, and PC-3. The antigen and mRNA levels of PAI-1 were down-regulated in cancer cells, especially in LNCaP and DU-145. In the presence of proinflammatory cytokines, an increase of PAI-1 mRNA levels was observed in PrEC, LNCaP and PC-3, but not in DU-145 cells. Treatment with demethylating agent, 5-aza-2’-deoxycytidine increased the level of PAI-1 transcript in DU-145 cells and restored the inducing effect of cytokines on PAI-1 expression. An aberrant methylation of PAI-1 promoter in DU-145 and LNCaP cells was shown by methylation-sensitive high resolution melting (MS-HRM) analysis. PAI-1 methylation was also significantly increased in tumor samples (23.2+/-1.7%) in comparison to adjacent non-tumor tissue (6.0+/-0.8%). Furthermore, the expression of uPA was increased in high invasive cell lines DU-145 and PC-3 in comparison to PrEC and low invasive LNCaP cells. MS-HRM analysis revealed aberrant methylation of uPA promoter in LNCaP cells, but not in PrEC, DU-145 and PC-3 cells, as well as in normal and prostate cancer tissue samples. In conclusion, the study shows that PAI-1 and uPA expressions were changed in opposite directions in high invasive prostate cancer cell lines resulting in a strong decrease of PAI-1/uPA ratio, which may indicate a shift towards proteolytic activities. Methylation of the PAI-1 gene is suggested as one of the molecular mechanisms involved in the cancer-associated down-regulation of the PAI-1 expression.
RESUMEN / SUMMARY: - Background: The incidence of prostate cancer is much lower in Asian men than in Western men. This study investigated whether prostate cancer is associated with prostatitis, benign prostatic hyperplasia (BPH), and other medical conditions in the low-incidence population. Methods: From the claims data obtained from the universal National Health Insurance of Taiwan, we identified 1184 patients with prostate cancer diagnosed from 1997 to 2008. Controls comprised 4736 men randomly selected from a cancer-free population. Both groups were 50 years of age or above. Medical histories between the two groups were compared. Results: Multivariate logistic regression analysis showed that prostatitis and BPH had stronger association with prostate cancer than the other medical conditions tested. Compared with men without prostatitis and BPH, a higher odds ratio (OR) for prostate cancer was associated with BPH (26.2, 95% confidence interval (CI) 20.8-33.0) than with prostatitis (10.5, 95% CI=3.36-32.7). Men with both conditions had an OR of 49.2 (95% CI=34.7-69.9). Conclusion: Men with prostate cancer have strong association with prostatitis and/or BPH. Prostatitis interacts with BPH, resulting in higher estimated relative risk of prostate cancer in men suffering from both conditions.

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TÍTULO / TITLE: - The Tumor-Suppressive Function of UNC5D and Its Repressed Expression in Renal Cell Carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Lu D; Dong D; Zhou Y; Lu M; Pang XW; Li Y; Tian XJ; Zhang Y; Zhang J

INSTITUCIÓN / INSTITUTION: - Authors’ Affiliations: Department of Immunology, Key Laboratory of Medical Immunology (Ministry of Health), Department of Pathology, School of Basic Medical Sciences, Peking University Health Science Center; and Department of Urology, Peking University Third Hospital, Beijing, China.

RESUMEN / SUMMARY: - PURPOSE: As a newly added member of the UNC5H receptors, the function of UNC5D/H4 in tumorigenesis remains poorly defined. The aim of this study was to examine the expression of UNC5D in primary renal cell carcinomas (RCC), analyze the mechanisms responsible for its downregulation in RCC, and assess its functional relevance to tumor growth and migration. EXPERIMENTAL DESIGN: Forty-four paired primary RCCs and corresponding adjacent noncancerous tissues were collected. The mRNA and protein expression level of UNC5D was assessed by reverse transcriptase-
PCR, real-time PCR, or immunohistochemistry. Epigenetic alterations in UNC5D promoter and LOH in the UNC5D locus were also analyzed. Ectopic expression of UNC5D in renal cancer cells with silenced expression of UNC5D was used for analysis of the biologic functions of UNC5D. RESULTS: UNC5D expression was attenuated in multiple carcinoma cell lines including renal cancer cells. Similar reduction was also observed in primary RCC tissues as compared with paired adjacent noncancerous tissues. Methylation-specific PCR showed hypermethylation in UNC5D promoter in a significant proportion (18 of 44) of tumor tissue (40.9%). LOH of UNC5D was observed in 13 of 44 patients with RCCs (29.5%). Restoration of UNC5D expression in renal cancer cells significantly inhibited cell proliferation, anchorage-dependent and -independent growth, as well as migration and invasion, whereas knockdown of UNC5D promoted cell growth. Furthermore, ectopic expression of UNC5D induced G2-M cell-cycle arrest. CONCLUSIONS: UNC5D is a functional tumor suppressor that is frequently downregulated in RCCs due to promoter hypermethylation and LOH. Clin Cancer Res; 19(11); 2883-92. ©2013 AACR.

[355]
TÍTULO / TITLE: - Baseline prostate-specific antigen measurements and subsequent prostate cancer risk in the Danish Diet, Cancer and Health cohort.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Larsen SB; Brasso K; Iversen P; Christensen J; Christiansen M; Carlsson S; Lilja H; Friis S; Tjonneland A; Dalton SO
INSTITUCIÓN / INSTITUTION: - Danish Cancer Society Research Center, Strandboulevarden 49, 2100 Copenhagen O, Denmark. Electronic address: benzon@cancer.dk.
RESUMEN / SUMMARY: - AIM: Although prostate-specific antigen (PSA) screening reduces mortality from prostate cancer, substantial over-diagnosis and subsequent overtreatment are concerns. Early screening of men for PSA may serve to stratify the male population by risk of future clinical prostate cancer. METHODS AND MATERIAL: Case-control study nested within the Danish ‘Diet, Cancer and Health’ cohort of 27,179 men aged 50-64 at enrolment. PSA measured in serum collected at cohort entry in 1993-1997 was used to evaluate prostate cancer risk diagnosed up to 14years after. We identified 911 prostate cancer cases in the Danish Cancer Registry through 31st December 2007 1:1 age-matched with cancer-free controls. Aggressive cancer was defined as T3 or Gleason score 7 or N1 or M1. Statistical analyses were based on conditional logistic regression with age as underlying time axis. RESULTS: Total PSA and free-to-total PSA ratio at baseline were strongly
associated with prostate cancer risk up to 14 years later. PSA was grouped in quintiles and free-to-total PSA ratio divided in three risk groups. The incidence rate ratio for prostate cancer was 150 (95% confidence interval, 72-310) among men with a total PSA in the highest quintile (>5.1 ng/ml) compared to the lowest (<0.80 ng/ml). The risk of aggressive cancer was highly elevated in men with a PSA level in the highest quintile. The results indicate that one-time measurement of PSA could be used in an individualised screening strategy, sparing a large proportion of men from further PSA-based screening.

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RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Tian TV; Tomavo N; Huot L; Flourens A; Bonnelye E; Flajollet S; Hot D; Leroy X; de Launoit Y; Duterque-Coquillaud M


RESUMEN / SUMMARY: Prostate cancer (PCa) is one of the major public health problems in Western countries. Recently, the TMPRSS2:ERG gene fusion, which results in the aberrant expression of the transcription factor ERG, has been shown to be the most common gene rearrangement in PCa. Previous studies have determined the contributions of this fusion in PCa disease initiation and/or progression in vitro and in vivo. In this study on TMPRSS2:ERG regulation in PCa, we used an androgen receptor and TMPRSS2:ERG fusion double-negative PCA cell model: PC3c. In three cell clones with different TMPRSS2:ERG expression levels, ectopic expression of the fusion resulted in significant induction of cell migration and invasion in a dose-dependent manner. In agreement with this phenotype, high-throughput microarray analysis revealed that a set of genes, functionally associated with cell motility and invasiveness, were deregulated in a dose-dependent manner in TMPRSS2:ERG-expressing cells. Importantly, we identified increased MMP9 (Metalloproteinase 9) and PLXNA2 (Plexin A2) expression in TMPRSS2:ERG-positive PCa samples, and their expression levels were significantly correlated with ERG expression in a PCa cohort. In line with these findings, there was evidence that TMPRSS2:ERG directly and positively regulates MMP9 and PLXNA2 expression in PC3c cells. Moreover, PLXNA2 upregulation contributed to TMPRSS2:ERG-mediated enhancements of PC3c cell migration and invasion. Furthermore, and importantly, PLXNA2 expression was upregulated in
metastatic PCa tumors compared with localized primary PCa tumors. This study provides novel insights into the role of the TMPRSS2:ERG fusion in PCa metastasis. Oncogene advance online publication, 27 May 2013; doi:10.1038/onc.2013.176.

[357]
TÍTULO / TITLE: - Results of hormone therapy as first-line treatment for high-risk prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
1097/MOU.0b013e328361f503
AUTORES / AUTHORS: - Mottet N
INSTITUCIÓN / INSTITUTION: - Urology Department, University Hospital Nord, St Etienne cedex 2, France.
RESUMEN / SUMMARY: - PURPOSE OF REVIEW: To assess the current place for androgen deprivation therapy as single modality in locally advanced nonmetastatic situations. RECENT FINDINGS: One standard of care for node negative locally advanced disease is a combination of external beam with androgen deprivation treatment. Several recent randomized trials have confirmed the key role of a local treatment combined to a systemic one in terms of specific and overall survival. The specific morbidity of this combined modality appears to be minimal. Retrospective data also suggest that a local treatment should be considered in case of positive nodes. Finally, the real place of immediate single hormonal treatment has also been clarified. The limited survival benefit has to be balanced with the side-effects. Therefore, this single modality should be limited to the most aggressive situations when no local treatment is planned. SUMMARY: Single hormonal treatment for nonmetastatic advanced prostate cancer appears to be limited to the few patients unfit or unwilling for a local treatment and having a high prostate-specific antigen and a short prostate-specific antigen doubling time. In all other situations, it might represent a clear undertreatment.

[358]
TÍTULO / TITLE: - Coffee and risk of prostate cancer incidence and mortality in the Cancer of the Prostate in Sweden Study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
1007/s10552-013-0234-9
AUTORES / AUTHORS: - Wilson KM; Balter K; Moller E; Adami HO; Andren O; Andersson SO; Gronberg H; Mucci LA
INSTITUCIÓN / INSTITUTION: - Department of Epidemiology, Harvard School of Public Health, 677 Huntington Ave, Boston, MA, 02115, USA, kwilson@hsph.harvard.edu.

RESUMEN / SUMMARY: - PURPOSE: Coffee intake has recently been associated with significantly lower risk of lethal and advanced prostate cancer in a US population. METHODS: We studied the association between coffee and prostate cancer risk in the population-based case-control study Cancer of the Prostate in Sweden. Dietary data were available for 1,499 cases and 1,112 controls. We calculated odds ratios (ORs) for the risk of prostate cancer in high versus low categories of coffee intake using logistic regression. We studied overall prostate cancer risk as well as risk of fatal, advanced, localized, high-grade, grade 7, and low-grade disease. RESULTS: Mean coffee intake was 3.1 cups per day among both cases and controls. Coffee intake was not associated with overall prostate cancer risk. Risk of fatal prostate cancer was inversely, but not statistically significantly, associated with coffee intake, with an odds ratio of 0.64 [95 % confidence interval (CI) 0.34-1.19, p value for linear trend = 0.81] for men consuming greater than 5 cups per day compared to men drinking less than 1 cup per day. The highest intake of coffee was associated nonsignificantly with lower risk of advanced disease (OR = 0.73, 95 % CI 0.41-1.30, p trend = 0.98) and associated significantly with lower risk of high-grade cancer (Gleason 8-10; OR = 0.50, 95 % CI 0.26-0.98, p trend = 0.13). Risk of localized, grade 7, and low-grade cancers was not associated with coffee intake. CONCLUSIONS: This study provides some support of an inverse association between coffee and lethal and high-grade prostate cancer.

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TÍTULO / TITLE: - Proteomic identification of angiomotin by ProteomeLab PF-2D and correlation with clinical outcome in human clear cell renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Yang J; Liu P; Tian M; Li Y; Chen W; Li X
INSTITUCIÓN / INSTITUTION: - Medical Oncology Department, The First Affiliated Hospital, College of Medicine, Xi’an Jiaotong University, Xi’an 710061, P.R. China.
RESUMEN / SUMMARY: - Identification of new therapeutic and prognostic biomarkers for clear cell renal cell carcinoma (ccRCC) is urgently required since most patients are in advanced stages of ccRCC at initial diagnosis and the recurrence rate is high. Differentially expressed proteins between the
ccRCC cell line RLC-310 and the normal renal cell line HK-2 were identified by a comparative proteomic approach based on a protein fractionation two-dimensional (PF-2D) liquid-phase fractionation system and capillary liquid chromatography electrospray ionization mass spectrometry/mass spectrometry (LC-ESI-MS/MS). Differentially expressed proteins (n=196) were identified. Of the 13 differentially expressed proteins newly discovered in ccRCC, angiomotin (Amot) was the focus of this study since its role in ccRCC progression has been obscure. The overexpression of Amot in ccRCC tissues was confirmed by comparing Amot expression in 18 primary ccRCC tissues and adjacent normal renal tissues (ANRT) using western blot analysis. Quantitative RT-PCR using 127 ccRCC tissues revealed that high levels of Amot transcripts were associated with poor differentiation, venous invasion and decreased survival (p<0.0001, <0.05 and <0.05). Multivariate analysis indicated that Amot transcript was an independent prognostic factor for the survival of ccRCC patients (p<0.05). These data suggest that Amot may serve as a novel prognostic factor of ccRCC.

[360]
TÍTULO / TITLE: - Concomitant loss of EAF2/U19 and Pten synergistically promotes prostate carcinogenesis in the mouse model.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1038/onc.2013.190
AUTORES / AUTHORS: - Ai J; Pascal LE; O'Malley KJ; Dar JA; Isharwal S; Qiao Z; Ren B; Rigatti LH; Dhir R; Xiao W; Nelson JB; Wang Z
INSTITUCIÓN / INSTITUTION: - Department of Urology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA.
RESUMEN / SUMMARY: - Multiple genetic alterations are associated with prostate carcinogenesis. Tumor-suppressor genes phosphatase and tensin homolog deleted on chromosome 10 (Pten) and androgen upregulated gene 19 (U19), which encodes ELL-associated factor 2 (EAF2), are frequently inactivated or downregulated in advanced prostate cancers. Previous studies showed that EAF2 knockout caused tumors in multiple organs and prostatic intraepithelial neoplasia (PIN) in mice. However, EAF2-knockout mice did not develop prostate cancer even at 2 years of age. To further define the roles of EAF2 in prostate carcinogenesis, we crossed the Pten+/− and EAF2+/− mice in the C57/BL6 background to generate EAF2−/−Pten+/−, Pten+/−, EAF2−/− and wild-type mice. The prostates from virgin male mice with the above four genotypes were analyzed at 7 weeks, 19 weeks and 12 months of age. Concomitant loss of EAF2 function and inactivation of one Pten allele induced spontaneous prostate cancer in 33% of the mice. Prostatic tissues from intact EAF2−/− Pten+/− mice exhibited higher levels of phospho-Akt, -p44/42 and microvessel density.
Moreover, phospho-Akt remained high after castration. Consistently, there was a synergistic increase in prostate epithelial proliferation in both intact and castrated EAF2-/Pten-/- mice. Using laser-capture microdissection coupled with real-time reverse transcription-PCR, we confirmed that co-downregulation of EAF2 and Pten occurred in >50% clinical prostate cancer specimens with Gleason scores of 8-9 (n=11), which is associated with poor prognosis. The above findings together demonstrated synergistic functional interactions and clinical relevance of concurrent EAF2 and Pten downregulation in prostate carcinogenesis. Oncogene advance online publication, 27 May 2013; doi:10.1038/onc.2013.190.
TÍTULO / TITLE: - Potential risk factors and outcomes of artificial urinary sphincter placement after radical cystectomy and orthotopic neobladder urinary diversion.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

   ●●Enlace al texto completo (gratuito o de pago) 1002/nau.22345

AUTORES / AUTHORS: - Vainrib M; Simma-Chiang V; Boyd SD; Ginsberg DA

INSTITUCIÓN / INSTITUTION: - University of Southern California, Los Angeles, California.

RESUMEN / SUMMARY: - AIMS: Stress urinary incontinence (SUI) is a known possibility after radical cystectomy (RC) and orthotopic neobladder (ONB) urinary diversion. We retrospectively reviewed the outcomes and complications of patients who underwent artificial urinary sphincter (AUS) placement for treatment of SUI and evaluated potential risk factors (PRFs) for AUS failure.

METHODS: Patients who underwent AUS placement after RC/ONB from 1994 to 2009 were identified. Variables evaluated included: demographics, cancer type, AUS characteristics, urinary incontinence (UI), revision procedures data, and PRFs for AUS failure. RESULTS: Demographic data was reviewed on 36 patients. Mean age at AUS placement was 72 (58-79) years. Mean time to AUS after RC/ONB was 28 (2-120) months. Mean follow up after AUS was 40 (2-132) months. TCC was the indication for RC in 94% of patients. The most commonly placed AUS cuff and reservoir size was 4.5 cm and 61-70 H2 O, respectively. Incontinence data was available in 29 patients. Pre-AUS placement 22, 3, and 4 patients were totally, daytime and nighttime only incontinent, respectively. Post-AUS placement, incontinence persisted in 5, 1, and 2 patients with total, daytime and nighttime incontinence, respectively. Prior to AUS placement 11/36 patients received chemotherapy and 10/36 had radiation. Mean time to the first revision/explantation due to UI/erosion/infection/malfunction was an average of 28 (3-96) months after AUS placement and occurred in 21/35 (60%) patients. There was no significant correlation noted between PRFs and UI pre-/post-AUS or between PRFs and the need for AUS revision. CONCLUSIONS: AUS is a safe, effective treatment with an acceptable complication rate for patients after RC/ONB with SUI. Neurourol. Urodynam. © 2012 Wiley Periodicals, Inc.

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[363]

TÍTULO / TITLE: - Classifying the Reasons Men Consider to be Important in Prostate-Specific Antigen (PSA) Testing Decisions: Evaluating Risks, Lay Beliefs, and Informed Decisions.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: McDowell ME; Occhipinti S; Chambers SK
INSTITUCIÓN / INSTITUTION: Griffith Health Institute, School of Applied Psychology, Griffith University, Mount Gravatt, QLD, 4111, Australia, M.McDowell@griffith.edu.au.

RESUMEN / SUMMARY: BACKGROUND: Despite uncertainty regarding the benefits of prostate cancer screening, many men have had a prostate-specific antigen (PSA) test. PURPOSE: This study aims to identify classes of reasons guiding men’s decisions about prostate cancer screening and predict reasoning approaches by family history and prior screening behaviour. METHODS: First-degree relatives of men with prostate cancer (n = 207) and men from the general population (n = 239) of Australia listed reasons they considered when deciding whether to have a PSA test. RESULTS: Responses were coded into 31 distinct categories. Latent class analysis identified three classes. The evaluation of risk information cues class (20.9 %) contained a greater number of men with a family history (compared with control and overcome cancer/risk class; 52.7 %). Informed decisions and health system class (26.5 %) included a lower proportion of men who had had a PSA test and greater proportions of highly educated and married men. CONCLUSION: Understanding the reasons underlying men's screening decisions may lead to a more effective information provision and decision support.

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TÍTULO / TITLE: Assessing treatment response after induction Bacillus Calmette-Guerin for carcinoma in situ of the urinary bladder: can post-induction random bladder biopsies be avoided?
RESUMEN / SUMMARY: OBJECTIVES: Patients diagnosed with bladder carcinoma in situ (CIS) and treated with intravesical Bacillus Calmette-Guerin (BCG) often undergo post-induction random bladder biopsies to assess treatment response. We sought to determine the correlation between post-induction urinary cytology/cystoscopy and histopathological findings obtained by random bladder biopsies. METHODS: Patients who were treated with BCG between 2006 and 2010 for CIS, had surveillance cystoscopy and cytology, and subsequently underwent random bladder biopsies were selected for analysis. Patients with a history of or concomitant urothelial cell carcinoma (UCC) stage...
T1 or higher were excluded. Cystoscopic findings were characterized as follows: negative - no mucosal erythema, raised lesions or papillary tumours; suspicious - mucosal erythema, but no raised lesions or papillary tumours; and positive - sessile or papillary tumours. The accuracy of cytology in predicting the results of subsequent random bladder biopsies was analysed. RESULTS: Of 21 patients included, surveillance cystoscopy findings were characterized as negative in nine, suspicious in seven and positive in five. Of 16 patients with negative/suspicious cystoscopy, 13 had agreement between cytology and biopsy, nine of whom were negative and four positive. Three of 16 patients had positive cytology, but negative biopsies; on further investigation of these three, one had CIS and two subsequent UCC. In the positive cystoscopy group, four of five patients had agreement between cytology and biopsy, two of whom were negative and two positive. One of the five patients had negative cytology, but a positive biopsy. CONCLUSION: Our data suggest foregoing random bladder biopsies in patients with negative urine cytology and no evidence of intravesical recurrence on cystoscopy following an induction course of BCG for CIS of the urinary bladder.

[365]

**TÍTULO / TITLE:** Minireview: androgen metabolism in castration-resistant prostate cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Sharifi N

**INSTITUCIÓN / INSTITUTION:** Department of Cancer Biology, Lerner Research Institute, Glickman Urological and Kidney Institute and Taussig Cancer Institute, Cleveland Clinic, Ohio 44195. sharifin@ccf.org.

**RESUMEN / SUMMARY:** The decades-old terminology of androgen independence has been replaced in recent years with castration-resistant prostate cancer. Biological and clinical evidence have together conspired to support the use of this revised terminology by demonstrating that in the vast majority of cases tumors are neither truly depleted of androgens, nor are they free of the requirement for androgens to sustain growth and progression. Abiraterone acetate, an androgen synthesis inhibitor, and enzalutamide, a potent androgen receptor antagonist, both exploit the continued requirement for androgens. A central question, given the therapeutic gains enabled by further suppression of the androgen axis with these newer agents, is whether there may be additional clinical benefit gained by moving the goal posts of androgen suppression even further. The answer lies in part with the mechanisms utilized by tumors that enable resistance to these therapies. The aims of this review
were to give a broad outline of steroidogenesis in prostate cancer and to 
highlight recent developments in understanding resistance to hormonal 
therapies.

[366]
**TÍTULO / TITLE:** - Gene fusions by chromothripsis of chromosome 5q in the VCaP prostate cancer cell line.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Teles Alves I; Hiltemann S; Hartjes T; van der Spek P; Stubbs A; Trapman J; Jenster G

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Josephine Nefkens Institute, Erasmus University Medical Center, Be 362ª, P.O. Box 2040, 3000 CA, Rotterdam, The Netherlands, i.telesalves@erasmusmc.nl

**RESUMEN / SUMMARY:** - The VCaP cell line is widely used in prostate cancer research as it is a unique model to study castrate resistant disease expressing high levels of the wild type androgen receptor and the TMPRSS2-ERG fusion transcript. Using next generation sequencing, we assembled the structural variations in VCaP genomic DNA and observed a massive number of genomic rearrangements along the q arm of chromosome 5, characteristic of chromothripsis. Chromothripsis is a recently recognized phenomenon characterized by extensive chromosomal shattering in a single catastrophic event, mainly detected in cancer cells. Various structural events identified on chromosome 5q of VCaP resulted in gene fusions. Out of the 18 gene fusion candidates tested, 15 were confirmed on genomic level. In our set of gene fusions, only rarely we observe microhomology flanking the breakpoints. On RNA level, only five transcripts were detected and NDUFAF2-MAST4 was the only resulting in an in-frame fusion transcript. Our data indicate that although a marker of genomic instability, chromothripsis might lead to only a limited number of functionally relevant fusion genes.

[367]
**TÍTULO / TITLE:** - Tissue expression of MLH1, PMS2, MSH2, and MSH6 proteins and prognostic value of microsatellite instability in Wilms tumor: experience of 45 cases.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Pediatr Hematol Oncol. 2013 May;30(4):273-84.
BACKGROUND: Although the importance of microsatellite instability (MSI) and mismatch repair genes (MMR) is strongly established in colorectal cancer seen in the Lynch syndrome, its significance has not been fully established in Wilms tumor (WT). The aim of this study was to determine the prognostic value of MSI and MMR proteins in WT. METHODS: This study included 45 pediatric cases with nephroblastoma. Protein expression was analyzed by immunohistochemistry of archival tissue sections. Real-time PCR melting analysis and fluorescence capillary electrophoresis (FCE) were performed to evaluate the MSI markers BAT25, BAT26, NR21, NR24, MONO27, penta D, and penta C in DNA extracted from tumor and normal tissues. RESULTS: Lower levels of MSI were observed in six cases (13.3%). There were no statistically significant correlations between MSI and some clinical prognostic factors such as stage of the tumors, and survival rates. Nineteen tumors (42.2%) showed loss of protein expression of MLH1, PMS2, MSH2, or MSH6. MMR protein defects were correlated with size (P = .021), and stage (P = .019) of the tumor, and survival rates (P < .01). Similarly MSI was also correlated with the size of the tumor (P = .046). CONCLUSIONS: This study showed that a small proportion of WT might be associated with the presence of MSI, as is the case with defects of DNA mismatch repair genes in the pathogenesis of WT. However, there was no concordance with the frequency of tissue expression of MMR proteins and MSI. These findings suggest that MMR genes may play an important role in the development of WT via different pathways.
RESUMEN / SUMMARY: - Background: Benign prostatic hyperplasia is one of the most common conditions in middle-aged and elderly males. Aim of the study: Investigate the biological effects and changes in the levels of relevant cellular factors and to elucidate the possible mechanism underlying the effects of low-frequency ultrasound combined with microbubble agents. Methods: Eighteen Male Beagle canines were divided into six groups randomly: Control group, 21kHz ultrasonic-treated group, 21kHz ultrasound and microbubble contrast agent-treated group, 1MHz ultrasonic-treated group, the 1MHz ultrasound and microbubble contrast agent-treated group, and the microbubble contrast agent-treated group. The changes of histological damage, mitochondria damage, cell apoptosis, biochemical markers, and levels of PSA, iNOS, and SOD were determined. Results: Significant tissue injury, mitochondria injury, and cell apoptosis were observed in 21kHz ultrasound and the microbubble contrast agent-treated group. Compared with the control and Sonovue-treated groups, the decreases in levels of PSA or increases in levels of iNOS and SOD in the other four groups were statistical significant (P<0.05). The lowest levels of PSA and the highest levels of iNOS and SOD were observed in the 21kHz ultrasound and Sonovue-treated group, and compared with the other five groups, the changes in levels of PSA, iNOS, and SOD were statistically significant (P<0.05). However, no significant changes in levels of AST, ALT, and BUN were observed between the six groups. Conclusions: Our results suggest that lower frequency ultrasound may have better effect on benign prostatic hyperplasia and microbubble contrast agent application further strengthen this biological effect.

[369]
TÍTULO / TITLE: - Effect of MLC leaf width on treatment adaptation and accuracy for concurrent irradiation of prostate and pelvic lymph nodes.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1118/1.4803499
AUTORES / AUTHORS: - Shang Q; Qi P; Ferjani S; Xia P
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Cleveland Clinic, Cleveland, Ohio 44195.
RESUMEN / SUMMARY: - Purpose: The aim of the study was to evaluate the impact of multileaf collimator (MLC) leaf width on treatment adaptation and delivery accuracy for concurrent treatment of the prostate and pelvic lymph nodes with intensity modulated radiation therapy (IMRT).Methods: Seventy-five kilovoltage cone beam CTs (KV-CBCT) from six patients were included for this retrospective study. For each patient, three different IMRT plans were created based on a planning CT using three different MLC leaf widths of 2.5, 5, and 10
mm, respectively. For each CBCT, the prostate displacement was determined by a dual image registration. Adaptive plans were created by shifting selected MLC leaf pairs to compensate for daily prostate movements. To evaluate the impact of MLC leaf width on the adaptive plan for each daily CBCT, three MLC shifted plans were created using three different leaf widths of MLCs (a total of 225 adaptive treatment plans). Selective dosimetric endpoints for the tumor volumes and organs at risk (OARs) were evaluated for these adaptive plans. Using the planning CT from a selected patient, MLC shifted plans for three hypothetical longitudinal shifts of 2, 4, and 8 mm were delivered on the three linear accelerators to test the deliverability of the shifted plans and to compare the dose accuracy of the shifted plans with the original IMRT plans.

Results: Adaptive plans from 2.5 and 5 mm MLCs had inadequate dose coverage to the prostate (D99 < 97%, or Dmean < 99% of the planned dose) in 6%-8% of the fractions, while adaptive plans from 10 mm MLC led to inadequate dose coverage to the prostate in 25.3% of the fractions. The average V56Gy of the prostate over the six patients was improved by 6.4% (1.6%-32.7%) and 5.8% (1.5%-35.7%) with adaptive plans from 2.5 and 5 mm MLCs, respectively, when compared with adaptive plans from 10 mm MLC. Pelvic lymph nodes were well covered for all MLC adaptive plans, as small differences were observed for D99, Dmean, and V50.4Gy. Similar OAR sparing could be achieved for the bladder and rectum with all three MLCs for treatment adaptation. The MLC shifted plans can be accurately delivered on all three linear accelerators with accuracy similar to their original IMRT plans, where gamma (3%/3 mm) passing rates were 99.6%, 93.0%, and 92.1% for 2.5, 5, and 10 mm MLCs, respectively. The percentages of pixels with dose differences between the measurement and calculation being less than 3% of the maximum dose were 85.9%, 82.5%, and 70.5% for the original IMRT plans from the three MLCs, respectively.

Conclusions: Dosimetric advantages associated with smaller MLC leaves were observed in terms of the coverage to the prostate, when the treatment was adapted to account for daily prostate movement for concurrent irradiation of the prostate and pelvic lymph nodes. The benefit of switching the MLC from 10 to 5 mm was significant (p << 0.01); however, switching the MLC from 5 to 2.5 mm would not gain significant (p = 0.15) improvement. IMRT plans with smaller MLC leaf widths achieved more accurate dose delivery.

[370]

**TITULO / TITLE:** - Ericifolin: a novel antitumor compound from allspice that silences androgen receptor in prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Carcinogenesis. 2013 May 9.

  ●●Enlace al texto completo (gratuito o de pago) [1093/carcin/bgt123](1093/carcin/bgt123)
Silencing of androgen receptor (AR) signaling is a specific and effective mechanism to cure cancer of the prostate (CaP). In this study, the isolation and characterization of a compound from the aromatic berries of Pimenta dioica (allspice) that silences AR is presented. Potential antitumor activities of an aqueous allspice extract (AAE) and a compound purified from the extract were tested on CaP cells. AAE inhibited tumor cell proliferation and colony formation (50% growth inhibition approximately 40-85 microg/ml) but not the viability of quiescent normal fibroblasts or non-tumorigenic prostate cells. In tumor cells, AAE inhibited cell cycle progression at G1/S, induced apoptosis or autophagy. Apoptosis was by caspase-dependent poly (ADP ribose) polymerase cleavage. A caspase-independent, apoptosis-inducing factor-mediated mechanism of apoptosis caused cell death in castration-resistant AR-positive or AR-negative CaP cells, such as CWR22RV1, PC-3 or DU145 cells. Treatment with AAE decreased the levels of AR messenger RNA (mRNA), protein and silenced AR activity in AR-positive cells. AR depletion was due to inhibition of AR promoter activity and mRNA stability. Delayed tumor growth (~55%) without measurable systemic toxicity was observed in LNCaP tumor-bearing mice treated with AAE by oral or intraperitoneal routes. LNCaP tumor tissues from AAE-treated mice revealed increased apoptosis as a potential mechanism of antitumor activity of AAE. The chemical identity of bioactive compound in AAE was established through multistep high-performance liquid chromatography fractionation, mass and Nuclear Magnetic Resonance spectroscopies. The compound, eugenol 5-O-beta-(6'-galloylglucopyranoside) or ericifolin (EF), showed antiproliferative, pro-apoptosis and anti-AR transcription activities. These results demonstrate a potential use of AAE and EF against prostate cancer.

[371]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Moris D; Vernadakis S; Zavvos V; Zavos G
INSTITUCIÓN / INSTITUTION: - 1 1st Department of Surgery Athens University School of Medicine “Laikon” General Hospital Athens, Greece 2 Department of General, Visceral and Transplantation Surgery University Hospital Essen
Essen, Germany 3 Transplantation Unit “Laikon” General Hospital Athens, Greece.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.02.098
AUTORES / AUTHORS: - Siegel C

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 2967/jnumed.112.115402
AUTORES / AUTHORS: - Keshari KR; Sai V; Wang ZJ; Vanbrocklin HF; Kurhanewicz J; Wilson DM
INSTITUCIÓN / INSTITUTION: - Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, California.
RESUMEN / SUMMARY: - Reduction and oxidation (redox) chemistry is increasingly implicated in cancer pathogenesis. To interrogate the redox status of prostate tumors noninvasively, we developed hyperpolarized [1-(13)C]dehydroascorbate ((13)C-DHA), the oxidized form of vitamin C, as an MR probe. In a model of transgenic adenocarcinoma of the mouse prostate (TRAMP), increased reduction of hyperpolarized (13)C-DHA to vitamin C was observed in tumor, as compared with normal prostate and surrounding benign tissue. We hypothesized that this difference was due to higher concentrations of glutathione and increased transport of hyperpolarized (13)C-DHA via the glucose transporters (GLUT1, GLUT3, and GLUT4) in TRAMP tumor. To test these hypotheses, hyperpolarized (13)C-DHA MR spectroscopy (MRS) and (18)F-FDG PET were applied as complementary technologies in the TRAMP model. METHODS: Late-stage TRAMP tumors (>4 cm(3)) were studied at similar time points (MR studies conducted < 24 h after PET) in fasting mice by (18)F-FDG PET and hyperpolarized (13)C-DHA MR imaging on a small-animal PET/CT scanner and a (1)H/(3)C 3-T MR scanner. PET data were processed
using open-source AMIDE software to compare the standardized uptake values of tumor with those of surrounding muscle, and (13)C-DHA MRS data were processed using custom software to compare the metabolite ratios (vitamin C/[vitamin C + (13)C-DHA]). After in vivo studies, the tumor glutathione concentrations were determined using a spectrophotometric assay, and thiol staining was performed using mercury orange. Real-time polymerase chain reaction was used to evaluate the relevant transporters GLUT1, GLUT3, and GLUT4 and vitamin C transporters SVCT1 and SVCT2. GLUT1 was also evaluated by immunohistochemistry. RESULTS: The average metabolite ratio was 0.28 +/- 0.02 in TRAMP tumor, versus 0.11 +/- 0.02 in surrounding benign tissue (n = 4), representing a 2.5-fold difference. The corresponding tumor-to-nontumor (18)F-FDG uptake ratio was 3.0. The total glutathione was 5.1 +/- 0.4 mM in tumor and 1.0 +/- 0.2 mM in normal prostate, whereas reduced glutathione was 2.0 +/- 0.3 mM and 0.8 +/- 0.3 mM, respectively, corresponding to a 2.5-fold difference. In TRAMP tumor, mercury orange staining demonstrated increased thiols. Real-time polymerase chain reaction showed no significant difference in GLUT1 messenger RNA between TRAMP tumor and normal prostate, with immunohistochemistry (anti-GLUT1) also showing comparable staining. CONCLUSION: Both hyperpolarized (13)C-DHA and (18)F-FDG provide similar tumor contrast in the TRAMP model. Our findings suggest that the mechanism of in vivo hyperpolarized (13)C-DHA reduction and the resulting tumor contrast correlates most strongly with glutathione concentration. In the TRAMP model, GLUT1 is not significantly upregulated and is unlikely to account for the contrast obtained using hyperpolarized (13)C-DHA or (18)F-FDG.

[374]
TÍTULO / TITLE: - Expression of Opa interacting protein 5 (OIP5) is associated with tumor stage and prognosis of clear cell renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.acthis.2013.03.008
AUTORES / AUTHORS: - Gong M; Xu Y; Dong W; Guo G; Ni W; Wang Y; Wang Y; An R
INSTITUCIÓN / INSTITUTION: - Department of Urological Surgery, The First Affiliated Hospital of Harbin Medical University, Harbin, China.
RESUMEN / SUMMARY: - Opa interacting protein 5 (OIP5), overexpressed in some types of human cancers, has been reported to be associated with the carcinogenesis of human cancer. However, the biological function and clinical significance of OIP5 in human Clear Cell Renal Cell Carcinoma (CCRCC)
remains unknown. In the present study, we found the expression of OIP5 was markedly upregulated in surgical CCRCC specimens and CCRCC cell lines. Immunohistochemical analysis revealed that paraffin-embedded archival CCRCC specimens exhibited higher levels of OIP5 expression than normal renal tissues. Further statistical analysis suggested the upregulation of OIP5 was positively correlated with the Fuhrman grade (P=0.02), T classification (P=0.015), N classification (P=0.018) and clinical stage (P=0.035). Also, patients with high OIP5 expression dramatically exhibited shorter survival time (P=0.001). In addition, the OIP5 expression was an independent prognostic marker of overall survival of CCRCC patients in a multivariate analysis (P=0.008). Experimentally, we demonstrated that silencing OIP5 in CCRCC cell lines by specific siRNA clearly inhibited cell growth. In conclusion, our findings suggested that OIP5 could be a valuable marker of CCRCC progression and prognosis, and a promising therapeutic target for CCRCC.

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[375]
TÍTULO / TITLE: - The conundrum of prostatic urethral involvement.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Ingimarsson JP; Seigne JD
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Dartmouth Hitchcock Medical Center, Norris Cotton Cancer Center, Geisel School of Medicine, Lebanon, NH 03756, USA.
RESUMEN / SUMMARY: - The presence and depth of urothelial cancer involvement in the prostatic urethra can significantly affect the management of a patient with non-muscle invasive bladder cancer. This article presents an overview of the incidence, diagnosis, management, and follow-up of urothelial cancer.

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[376]
TÍTULO / TITLE: - In vitro and in vivo growth inhibition of prostate cancer by the small molecule imiquimod.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Han JH; Lee J; Jeon SJ; Choi ES; Cho SD; Kim BY; Kim DJ; Park JH; Park JH
INSTITUCIÓN / INSTITUTION: - Department of Laboratory Animal Medicine, College of Veterinary Medicine, Seoul National University, Seoul 151742, Republic of Korea.

RESUMEN / SUMMARY: - Prostate cancer is the second leading cause of cancer death in men worldwide. In the present study, we examined in vitro and in vivo antitumor effect of the small molecule imiquimod, also known as a TLR7 agonist, against prostate cancer. Imiquimod inhibited the growth of mouse (TRAMP-C2) and human (PC-3) prostate cancer cells. Treatment with imiquimod induced cell cycle arrest at the G2/M phase in TRAMP-C2 cells, confirmed by the changes of G2/M checkpoint regulators such as reduction of cyclin B1 expression and increase of phospho-CDC2 and p21 in TRAMP-C2 cells treated with imiquimod. Flow cytometry and western blot analysis revealed that imiquimod induced direct apoptosis in TRAMP-C2 cells via a mitochondrial-dependent pathway. Intratumoral injection with imiquimod reduced significantly tumor growth and increased apoptotic cells in mice subcutaneously implanted with TRAMP-C2 cells. Our results indicate that imiquimod can be an alternative therapeutic for locally generated prostate cancer.

[377]

TÍTULO / TITLE: - beta-Ionone Induces Cell Cycle Arrest and Apoptosis in Human Prostate Tumor Cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Jones S; Fernandes NV; Yeganehjoo H; Katuru R; Qu H; Yu Z; Mo H

INSTITUCIÓN / INSTITUTION: - a Department of Nutrition and Food Sciences, Texas Woman's University, Denton, Texas, USA.

RESUMEN / SUMMARY: - 3-Hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase is the rate-limiting activity in the mevalonate pathway that provides essential intermediates for posttranslational modification of growth-associated proteins. Assorted dietary isoprenoids found in plant foods suppress HMG CoA reductase and have cancer chemopreventive activity. beta-Ionone, a cyclic sesquiterpene and an end-ring analog of beta-carotene, induced concentration-dependent inhibition of the proliferation of human DU145 (IC50 = 210 mumol/L) and LNCaP (IC50 = 130 mumol/L) prostate carcinoma cells and PC-3 prostate adenocarcinoma cells (IC50 = 130 mumol/L). Concomitantly, beta-ionone-induced apoptosis and cell cycle arrest at the G1 phase in DU145 and PC-3 cells were shown by fluorescence microscopy, flow cytometry, and TUNEL reaction, and downregulation of cyclin-dependent kinase 4 (Cdk4) and cyclin D1
proteins. Growth suppression was accompanied by beta-ionone-induced downregulation of reductase protein. A blend of beta-ionone (150 mumol/L) and trans, trans-farnesol (25 mumol/L), an acyclic sesquiterpene that putatively initiates the degradation of reductase, suppressed the net growth of DU145 cells by 73%, an impact exceeding the sum of those of beta-ionone (36%) and farnesol (22%), suggesting a synergistic effect. beta-ionone, individually or in combination with other HMG CoA reductase suppressors, may have potential in prostate cancer chemoprevention and/or therapy.

[378]

**TÍTULO / TITLE:** - Platinum-Based Chemotherapy for Variant Castrate-Resistant Prostate Cancer.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**REVISTA / JOURNAL:** - Clin Cancer Res. 2013 May 6.

**AUTORES / AUTHORS:** - Aparicio AM; Harzstark A; Corn PG; Wen S; Araujo J; Tu SM; Pagliaro L; Kim J; Millikan RE; Ryan CJ; Tannir NM; Zurita A; Mathew P; Arap W; Troncoso P; Thall P; Logothetis CJ
**INSTITUCIÓN / INSTITUTION:** - Genitourinary Medical Oncology, UT MD Anderson Cancer Center.
**RESUMEN / SUMMARY:** - PURPOSE: Clinical features characteristic of small-cell prostate carcinoma (SCPC), (“anaplastic”) often emerge during the progression of prostate cancer. We sought to determine the efficacy of platinum-based chemotherapy in patients meeting at least one of seven prospectively defined “anaplastic” clinical criteria, including exclusive visceral or predominantly lytic bone metastases, bulky tumor masses, low PSA levels relative to tumor burden or short response to androgen deprivation therapy. EXPERIMENTAL DESIGN: A 120-patient phase II trial of frontline carboplatin and docetaxel (CD) and second-line etoposide and cisplatin (EP) was designed to provide reliable clinical response estimates under a Bayesian probability model with early stopping rules in place for futility and toxicity. RESULTS: Seventy-four of 113 (65.4%) and 24 of 71 (33.8%) were progression free after 4 cycles of CD and EP, respectively. Median overall survival (OS) was 16 months (95% CI, 13.6-19.0 months). Of the 7 “anaplastic” criteria, bulky tumor mass was significantly associated with poor outcome. Lactic acid dehydrogenase (LDH) strongly predicted for OS and rapid progression. Serum carcinoembryonic antigen (CEA) concentration strongly predicted OS but not rapid progression. Neuroendocrine markers did not predict outcome or response to therapy. CONCLUSION: Our findings support the hypothesis that patients with “anaplastic” prostate cancer are a recognizable subset characterized by a high response rate of short duration to platinum-containing
chemotherapies, similar to SCPC. Our results suggest that CEA is useful for selecting therapy in men with CRPC and consolidative therapies to bulky high-grade tumor masses should be considered in this patient population.

[379]

TÍTULO / TITLE: - To combine or not combine: the role of radiotherapy and targeted agents in the treatment for renal cell carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Weiss C; Schulze B; Ottinger A; Rodel C

INSTITUCIÓN / INSTITUTION: - Department of Radiation Therapy and Oncology, Goethe University, Frankfurt, Germany, weiss.christian@hotmail.com

RESUMEN / SUMMARY: - INTRODUCTION: Renal cell carcinoma is counted among the most resistant tumors to chemotherapy and radiotherapy, respectively. However, therapeutic options expanded since the introduction of molecular agents, targeting specific pathways such as the vascular endothelial growth factor (VEGF)-alpha, the VEGF receptor (VEGFR), or the mammalian target of rapamycin (mTOR) pathway. These new agents almost doubled the time to tumor progression and in some trials even improved overall survival. Against this background, the role of local treatment strategies in metastasized or inoperable primary renal cell carcinoma has to be redefined. With the onset of new technical developments in radiotherapy and the possibility to precisely deliver higher doses per fraction, encouraging response and control rates have been reported for kidney cancer, supporting a possible role for irradiation in this setting. This overview summarizes the preclinical data and clinical experiences of modern radiotherapy with focus on possible synergies and toxicities when combined with molecular targeted agents. METHODS: The available literature on preclinical and clinical data comprising prospective trials, retrospective analyses and case reports was reviewed. CONCLUSION: With the recent developments in stereotactic and image-guided radiotherapy, encouraging data concerning local control in the treatment for metastasized renal cell carcinoma have been generated and are therefore recommended whenever possible. It seems that with these high-precision irradiation schedules, the combination with targeted agents is feasible with no increase in severe adverse events. Nevertheless, the addition of molecular targeted drugs to radiotherapy outside of approved regimens or clinical trials warrants careful consideration for every single case.

[380]
Plk1-Dependent Microtubule Dynamics Promotes Androgen Receptor Signaling in Prostate Cancer.

**RESUMEN / SUMMARY:**
Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Hou X; Li Z; Huang W; Li J; Staiger C; Kuang S; Ratliff T; Liu X

**INSTITUCIÓN / INSTITUTION:** - Department of Biochemistry, Purdue University, West Lafayette, Indiana; Department of Neurosurgery, Provincial Hospital affiliated to Shandong University, Jinan, China.

**RESUMEN / SUMMARY:**
BACKGROUND: The androgen receptor (AR) signaling continues to be essential in castrate-resistant prostate cancer (CRPC). Taxel-based chemotherapy is the current standard treatment for CRPC patients. Unfortunately, almost all patients eventually develop resistance toward this chemotherapy. Significantly, it was recently found that the anti-tumor effect of paclitaxel in CRPC is due to its inhibition of AR activity via its inhibition of microtubule dynamics. Polo-like kinase 1 (Plk1), a critical regulator in many cell cycle events, is elevated in prostate cancer (PCa) and linked to tumor grades. Of note, we have previously shown that Plk1 phosphorylates CLIP-170 and p150Glued, two important regulators of microtubule dynamics. METHODS: We compared paclitaxel-mediated phenotypes (inhibition of the AR signaling, decrease of microtubule dynamics and cell death) of PCa cells expressing different forms of CLIP-170 and p150Glued with different Plk1 phosphorylation states. RESULTS: We show that Plk1 phosphorylation of CLIP-170 and p150Glued affects cellular responses to paclitaxel. Expression of Plk1-unphosphorylatable mutants of CLIP-170 and p150Glued results in increased paclitaxel-induced apoptosis, increased protein degradation of the AR, and decreased nuclear accumulation of the AR in response to androgen in prostate cancer cells. Finally, we show that cells expressing unphosphorylatable mutants of CLIP-170 have defective microtubule dynamics, thus providing a new mechanism to understand how Plk1-associated kinase activity promotes constitutive activation of AR signaling in CRPC. CONCLUSIONS: Our data suggest that a combination of inhibition of Plk1 and paclitaxel might be a novel avenue for treatment of CRPC. Prostate 9999: XX-XX. © 2013 Wiley Periodicals, Inc.

Immunohistochemical Expression of ERG in the Molecular Epidemiology of Fatal Prostate Cancer Study.

**RESUMEN / SUMMARY:**
Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:**

**INSTITUCIÓN / INSTITUTION:**

**RESUMEN / SUMMARY:**

**TÍTULO / TITLE:** Central body fat distribution associates with unfavorable renal hemodynamics independent of body mass index.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Kwakernaak AJ; Zelle DM; Bakker SJ; Navis G

**INSTITUCIÓN / INSTITUTION:** Department of Medicine, Division of Nephrology, University of Groningen, University Medical Center Groningen, The Netherlands.

**RESUMEN / SUMMARY:** Central distribution of body fat is associated with a higher risk of renal disease, but whether it is the distribution pattern or the
overall excess weight that underlies this association is not well understood. Here, we studied the association between waist-to-hip ratio (WHR), which reflects central adiposity, and renal hemodynamics in 315 healthy persons with a mean body mass index (BMI) of 24.9 kg/m(2) and a mean (125)-iothalamate GFR of 109 ml/min per 1.73 m(2). In multivariate analyses, WHR was associated with lower GFR, lower effective renal plasma flow, and higher filtration fraction, even after adjustment for sex, age, mean arterial pressure, and BMI. Multivariate models produced similar results regardless of whether the hemodynamic measures were indexed to body surface area. Thus, these results suggest that central body fat distribution, independent of BMI, is associated with an unfavorable pattern of renal hemodynamic measures that could underlie the increased renal risk reported in observational studies.

[383]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.eururo.2013.03.034
AUTORES / AUTHORS: - Sun M; Becker A; Tian Z; Roghmann F; Abdollah F; Larouche A; Karakiewicz PI; Trinh QD
INSTITUCIÓN / INSTITUTION: - Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, Canada; Department of Public Health, Faculty of Medicine, University of Montreal, Montreal, Canada. Electronic address: mcw.sun@umontreal.ca.
RESUMEN / SUMMARY: - BACKGROUND: For elderly individuals with localized renal cell carcinoma (RCC), surgical intervention remains the primary treatment option but may not benefit patients with limited life expectancy. OBJECTIVE: To calculate the trade-offs between surgical excision and nonsurgical management (NSM) with respect to competing causes of mortality. DESIGN, SETTING, AND PARTICIPANTS: Relying on a cohort of Medicare beneficiaries, all patients with nonmetastatic node-negative T1 RCC between 1988 and 2005 were abstracted. INTERVENTION: All patients were treated with partial nephrectomy (PN), radical nephrectomy (RN), or NSM. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Cancer-specific mortality (CSM) and other-cause mortality (OCM) rates were modeled through competing-risks regression methodologies. Instrumental variable analysis was used to account for the potential biases associated with measured and unmeasured confounders. RESULTS AND LIMITATIONS: A total of 10 595 patients were identified. In
instrumental variable analysis, patients treated with PN (hazard ratio [HR]: 0.45; 95% confidence interval [CI], 0.24-0.83; p=0.01) or RN (HR: 0.58; 95% CI, 0.35-0.96; p=0.03) had a significantly lower risk of CSM than those treated with NSM. In subanalyses restricted to patients >/=75 yr, the instrumental variable analysis failed to detect any statistically significant difference between PN (HR: 0.48; p=0.1) or RN (HR: 0.57; p=0.1) relative to NSM with respect to CSM. Similar trends were observed in T1a RCC only. CONCLUSIONS: PN or RN is associated with a reduction of CSM among older patients diagnosed with localized RCC, compared with NSM. The same benefit failed to reach statistical significance among patients >/=75 yr. The harms of surgery need to be weighed against the marginal survival benefit for some patients.
TITULO / TITLE: - Formalin Disinfection of Biopsy Needle Minimizes the Risk of Sepsis Following Prostate Biopsy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Issa MM; Al-Qassab UA; Hall J; Ritenour CW; Petros JA; Sullivan JW

INSTITUCIÓN / INSTITUTION: - Department of Urology, Veterans Affairs Medical Center, Atlanta, GA; Department of Urology, Emory University School of Medicine, Atlanta, GA. Electronic address: issa@emory.edu.

RESUMEN / SUMMARY: - PURPOSE: We describe a simple and effective method to reduce the risk of infection following prostate biopsy. MATERIALS AND METHODS: A total of 1,642 consecutive prostate biopsy procedures during a four-year period (2008-2012) were included in the study. Inclusion criteria consisted of pre-biopsy negative urine culture, bisacodyl enema and fluoroquinolone antibiotics (3 days). Formalin (10%) was used to disinfect the needle tip after each biopsy core. All patients were monitored for post-biopsy infection. The rate of infection was compared to that of a historical series of 990 procedures. Two ex-vivo experiments were conducted to test the disinfectant effectiveness of formalin against FQ-resistant E. coli, and another experiment to quantify formalin exposure. RESULTS: Post-biopsy clinical sepsis with positive urine and blood cultures (quinolone-resistant E. coli) developed in two patients (0.122%). Both were hospitalized, treated with IV antibiotics and had full recovery without long-term sequelae. Three additional patients (0.183%) developed mild uncomplicated urinary infection. All were treated with outpatient oral antibiotics and had complete recovery. The overall rate of urinary infection and sepsis using formalin disinfection was approximately one-third of that of a prior series (0.30% versus 0.80%, p=0.13). Ex-vivo experiments showed complete lack of growth of FQ-resistant E. coli on blood and MacConkey agars following exposure to formalin. The amount of formalin exposure was negligible and well within the EPA’s safe parameter. CONCLUSIONS: Formalin disinfection of the biopsy needle after each prostate biopsy core is associated with low incidence of urinary infection and sepsis. The technique is simple, effective and cost-neutral.

[386]

- CASTELLANO -

TITULO / TITLE: Correlacion del cociente PSA complex/PSA total con el cociente PSA libre/PSA total, sensibilidad y especificidad de ambos marcadores para el diagnostico del cancer de prostata.
**TÍTULO / TITLE:** Correlation between the Complex PSA/total PSA Ratio and the Free PSA/total PSA Ratio, Sensitivity and Specificity of Both Markers for the Diagnosis of Prostate Cancer.

**RESUMEN / SUMMARY:**

Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1016/j.acuro.2012.11.014

**AUTORES / AUTHORS:** Perez-Lanzac-Lorca A; Barco-Sanchez A; Romero E; Martinez-Peinado A; Lopez-Elorza F; Sanchez-Sanchez E; Alvarez-Ossorio-Fernandez JL; Castineiras-Fernandez J

**INSTITUCIÓN / INSTITUTION:** Servicio de Urología, Hospital Universitario Puerta del Mar, Cadiz, España. Electronic address: albertoperezlanzac@gmail.com.

**RESUMEN / SUMMARY:**

**OBJECTIVE:** To compare the behaviour of the PSA complex/PSA total percentage (PSAc%) against the PSA free/PSA total (PSAl%) and analyse both markers for their usefulness in diagnosing prostate cancer. **MATERIAL AND METHODS:** We measured total PSA (PSAt), free PSA (PSAl), complex PSA (PSAc), PSAl% and PSAc% levels in 158 patients. Of these, 98 (62%) were biopsied for presenting PSAt>/=3ng/dl and PSAl%<20, PSAt>10, suspicious rectal examination or suspicious ultrasound node. We performed linear regression and Passing-Bablok regression analyses. The ROC curves were calculated to study the sensitivity and specificity of PSAl% and PSAc% and were compared to each other. The prostate cancer diagnoses were analysed by PSAl% and PSAc% by applying the chi2 test. **RESULTS:** The correlation coefficient (r) was good (0.7447, P<.0001), and the index of determination (r2) was 0.5. The result of the Passing-Bablok analysis was a slope of 1.658 (1.452 to 1.897) and an intersection of 2.044 (-0.936 to 5.393). The optimal cutoff for PSAl% (<14.7854) showed a sensitivity of 89.29% [95% CI, 0.642-0.823] and a specificity of 54.29% (95% CI, 0.642-0.823). The optimal cutoff for PSAc% (>89.7796) had a sensitivity of 71.43% (95% CI, 0.616-0.802) and a specificity of 71.43% (95% CI, 0.616-0.802). There were no significant differences when comparing the areas under the curve of both markers (P=.59). The PPV of PSAl% was less than that of PSAc% (45.7% vs. 71%). **CONCLUSION:** There was a good correlation between PSAl% and PSAc%. PSAc% has demonstrated greater specificity and efficacy than PSAl% in the diagnosis of prostate cancer.

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[387]

**TÍTULO / TITLE:** First (18)F-labeled ligand for PET imaging of uPAR: In vivo studies in human prostate cancer xenografts.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

292
●●Enlace al texto completo (gratuito o de pago)
1016/j.nucmedbio.2013.03.001

AUTORES / AUTHORS: - Persson M; Liu H; Madsen J; Cheng Z; Kjaer A

INSTITUCIÓN / INSTITUTION: - The Danish-Chinese Center for Proteases and Cancer, Virtual center; Department of Clinical Physiology, Nuclear Medicine and PET, Center for Diagnostic Investigations, Rigshospitalet, Copenhagen, Denmark; Cluster for Molecular Imaging, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark; Department of Radiology, Molecular Imaging Program at Stanford (MIPS), Bio-X Program, Stanford University, Stanford, CA 94305.

RESUMEN / SUMMARY: - Urokinase-type plasminogen activator receptor (uPAR) is overexpressed in human prostate cancer and uPAR has been found to be associated with metastatic disease and poor prognosis. AE105 is a small linear peptide with high binding affinity to uPAR. We synthesized an N-terminal NOTA-conjugated version (NOTA-AE105) for development of the first (18)F-labeled uPAR positron-emission-tomography PET ligand using the Al(18)F radiolabeling method. In this study, the potential of (18)F-AlF-NOTA-AE105 to specifically target uPAR-positive prostate tumors was investigated. METHODS: NOTA-conjugated AE105 was synthesized and radiolabeled with (18)F-AlF according to a recently published optimized protocol. The labeled product was purified by reverse phase high performance liquid chromatography RP-HPLC. The tumor targeting properties were evaluated in mice with subcutaneously inoculated PC-3 xenografts using small animal PET and ex vivo biodistribution studies. uPAR-binding specificity was studied by coinjection of an excess of a uPAR antagonist peptide AE105 analogue (AE152). RESULTS: NOTA-AE105 was labeled with (18)F-AlF in high radiochemical purity (>92%) and yield (92.7%) and resulted in a specific activity of greater than 20GBq/mumol. A high and specific tumor uptake was found. At 1h post injection, the uptake of (18)F-AlF-NOTA-AE105 in PC-3 tumors was 4.22+/−0.13%ID/g. uPAR-binding specificity was demonstrated by a reduced uptake of (18)F-AlF-NOTA-AE105 after coinjection of a blocking dose of uPAR antagonist at all three time points investigated. Good tumor-to-background ratio was observed with small animal PET and confirmed in the biodistribution analysis. Ex vivo uPAR expression analysis on extracted tumors confirmed human uPAR expression that correlated close with tumor uptake of (18)F-AlF-NOTA-AE105. CONCLUSION: The first (18)F-labeled uPAR PET ligand, (18)F-AlF-NOTA-AE105, has successfully been prepared and effectively visualized noninvasively uPAR positive prostate cancer. The favorable in vivo kinetics and easy production method facilitate its future clinical translation for identification of prostate cancer patients with an invasive phenotype and poor prognosis.
TÍTULO / TITLE: Re: transition zone prostate cancer: detection and localization with 3-t multiparametric MR imaging.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Taneja SS

INSTITUCIÓN / INSTITUTION: Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.

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TÍTULO / TITLE: High Circulating Estrogens and Selective Expression of ERbeta in Prostate Tumors: Implications for Racial Disparity of Prostate Cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Abd Elmageed ZY; Moroz K; Srivastav SK; Fang Z; Crawford BE; Moparty K; Thomas R; Abdel-Mageed AB

INSTITUCIÓN / INSTITUTION: Departments of Urology, Tulane University Health Science Center, New Orleans, LA, USA.

RESUMEN / SUMMARY: Although estrogen receptor beta (ERbeta) has been implicated in prostate cancer (PCa) progression, its potential role in health disparity of PCa remains elusive. The objective of this study was to examine serum estrogens and prostate tumor ERbeta expression and examine their correlation with clinical and pathological parameters in African American (AA) versus Caucasian American (CA) men. The circulating 17beta-Estradiol (E2) was measured by EIA in blood procured from racially stratified normal subjects and PCa patients. Differential expression profile analysis of ERbeta was analyzed by quantitative IHC using ethnicity-based tissue microarray encompassing 300 PCa tissue cores. In situ ERbeta expression was validated by qRT-PCR in matched microdissected normal prostate epithelium and tumor cells and datasets extracted from independent cohorts. Circulating E2 levels are significantly elevated in PCa patients in comparison to normal age-matched subjects. However, further analysis an increase in blood E2 levels in AA-men, both normal and PCa, than in counterparts of CA decent. Histoscore (HS) analysis reveals intense nuclear immunoreactivity for ERbeta in tumor cores of AA than in CA men. Gene expression analysis in microdissected tumors corroborated the biracial differences in ERbeta expression. Gene expression analysis from independent cohort datasets revealed correlation between
ERbeta expression and PCa progression. However, unlike in CA men, adjusted multivariate analysis showed that ERbeta expression correlates with age at diagnosis and low PSA recurrence-free survival in AA men. Taken together, our results suggest that 17beta-Estradiol-ERbeta axis may have potential clinical utility in PCa diagnosis and clinical outcome among AA men.
**TÍTULO / TITLE:** - Words of wisdom: Re: Population based study of long-term rates of surgery for urinary incontinence after radical prostatectomy for prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


  ●●Enlace al texto completo (gratuito o de pago) 1016/j.eururo.2013.02.017

**AUTORES / AUTHORS:** - Madersbacher S

**INSTITUCIÓN / INSTITUTION:** - Donauspital - SMZO, Urology, Langobardenstrasse 122, Wien 1220, Austria. Stephan.madersbacher@wienkav.at

[392]

**TÍTULO / TITLE:** - Coffee consumption and the risk of overall and fatal prostate cancer in the NIH-AARP Diet and Health Study.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Cancer Causes Control. 2013 May 17.

  ●●Enlace al texto completo (gratuito o de pago) 1007/s10552-013-0229-6

**AUTORES / AUTHORS:** - Bosire C; Stampfer MJ; Subar AF; Wilson KM; Park Y; Sinha R

**INSTITUCIÓN / INSTITUTION:** - Department of Nutrition, Harvard School of Public Health, 655 Huntington Avenue, Boston, MA, 02115, USA, bosirec@mail.harvard.edu.

**RESUMEN / SUMMARY:** - PURPOSE: Evidence on the association between coffee consumption and prostate cancer risk is inconsistent; furthermore, few studies have examined the relationship between coffee consumption and fatal prostate cancer. The aim of this study was to investigate whether coffee intake is associated with the risk of overall and fatal prostate cancer. METHODS: We conducted a prospective analysis among 288,391 men in the National Institutes of Health AARP Diet and Health Study who were between 50 and 71 years old at baseline in 1995-1996. Coffee consumption was assessed at baseline. Cox proportional hazards models were used to calculate the age- and multivariable-adjusted hazard ratios (HR)s and 95 % confidence intervals (CIs). RESULTS: Over 11 years of follow-up, 23,335 cases of prostate cancer were ascertained, including 2,927 advanced and 917 fatal cases. Coffee consumption was not significantly associated with prostate cancer risk. The multivariable-adjusted HRs (95 % CI), comparing those who drank six or more cups per day to nondrinker, were as follows: 0.94 (0.86-1.02), p trend = 0.08 for overall prostate cancer, 1.13 (0.91-1.40), p trend = 0.62 for advanced prostate cancer, and 0.79 (0.53-1.17), p trend = 0.20 for fatal prostate cancer. The findings remained nonsignificant when we stratified by prostate-specific antigen testing history or
restricted to nonsmokers. CONCLUSIONS: We found no statistically significant association between coffee consumption and the risk of overall, advanced, or fatal prostate cancer in this cohort, though a modest reduction in risk could not be excluded.

[393]
TÍTULO / TITLE: - Risk Factors for Renal Cell Carcinoma in the Vitamin and Lifestyle (VITAL) Study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Macleod LC; Hotaling JM; Wright JL; Davenport MT; Gore JL; Harper J; White E
INSTITUCIÓN / INSTITUTION: - University of Washington Medical Center, Department of Urology, 1959 NE Pacific St., BB-1121, Seattle WA 98195, phone 206.535.5886 or 206.685.1982, fax 206.543.3272.
RESUMEN / SUMMARY: - PURPOSE: The incidence of renal cell carcinoma (RCC) is increasing worldwide. Cited risk factors include obesity, smoking and hypertension, but few others have been confirmed by prospective studies. We used a prospective cohort to validate established RCC risk factors and to evaluate more controversial risk factors for incident RCC.
MATERIALS/METHODS: 77,260 residents of Washington aged 50-76 years completed a questionnaire between 2000-2002 on demographic, lifestyle and health data. Incident RCC cases were determined through linkage to the regional cancer registry through Dec 31, 2009. Multivariate methods using covariates and cut offs selected a priori analyzed the association between RCC and previously studied factors related to lifestyle (body mass index [BMI], smoking, alcohol/fruit/vegetable consumption) and health (hypertension, diabetes, kidney disease, viral hepatitis). RESULTS: There were 249 incident cases of RCC. Independent RCC risk factors in the fully adjusted model with HR and 95% CIs were: BMI (HR 1.71, CI 1.06, 2.79, for >=35 kg/m2 vs. <25 kg/m2), smoking (HR 1.67, CI 1.16, 2.42, for >=37.5 pack-years vs. none), hypertension (HR 1.70, CI 1.30, 2.22), kidney disease (HR 2.58, CI 1.21, 5.50), viral hepatitis (HR 1.80, CI 1.03, 3.14). Diabetes was associated with RCC (HR 1.83, CI 1.26, 2.65) in a base model adjusting for age and gender, but not in the multivariate model. We found no association between alcohol, fruit, or vegetable intake and RCC. CONCLUSIONS: We identified significant association between RCC and obesity, smoking, hypertension, renal disease and viral hepatitis. Identification of risk factors offers an opportunity for targeted education and intervention.
Testicular hemangioma: a series of 8 cases.

RESUMEN / SUMMARY: Testicular hemangioma is a very rare neoplasm with only 25 cases reported in the English literature. We describe 8 cases of testicular hemangioma encountered at our institution between 1992 and 2012. Of the 7 consult cases, 4 were malignant, 1 a Leydig cell tumor, and 2 were recognized as hemangiomas. The patients’ ages ranged from 9 to 54 years (mean 32; median 30). Seven patients presented with self-detected palpable masses, and 2 patients reported pain. Six hemangiomas involved the right testis, and 2 were left sided. Ultrasonography recognized hypervascularity in 3 cases. History of pelvic irradiation, chemotherapy, and remote scrotal trauma was present in 3 patients. Preoperative serum tumor markers were negative (2/2 cases). The average size was 1.7 cm (median 1.8; range, 0.5 to 3.0). Six cases were infiltrative within the testis and entrapped benign seminiferous tubules, and 3 tumors invaded the tunica albuginea. Three hemangiomas were epithelioid, 2 anastomosing, 1 cellular capillary, 1 capillary, and 1 cavernous. Mitoses were sparse in all but 1 case, which reached up to 5 per 10 HPF. In 6 cases, seminiferous tubules adjacent to the hemangioma were atrophic without spermatogenesis. Immunohistochemical analysis was performed in 6 cases, and tumors stained with CD31, CD34, FVIII-related protein, and FLI-1 but not with pancytokeratin AE1/3, epithelial membrane antigen, keratin 8/18, placental alkaline phosphatase, human herpes virus 8, human chorionic gonadotropin, c-kit, melan-A, or p53. In cases with follow-up, there were no recurrences in 7 patients (mean 21 mo; median 12 mo; range, 1 to 72 mo). In summary, testicular hemangioma is a rare neoplasm with different morphologies having in common an infiltrative growth pattern with entrapment of seminiferous tubules, which should not be considered a feature of malignancy. Clinical and radiologic findings may preoperatively suggest a vascular tumor.

New agents for bacillus Calmette-Guerin-refractory bladder cancer.

Bacillus Calmette-Guerin has been established as the primary treatment of high-risk non-muscle invasive bladder cancer. If patients do not respond or later recur, the most reliable treatment option is cystectomy. For those who are unwilling or unable to undergo this significant procedure, there is a multitude of alternative intravesical therapies. This article provides an overview of treatment options for patients with non-muscle invasive bladder cancer who have failed intravesical bacillus Calmette-Guerin therapy. It includes information on recent and ongoing trials and serves as a guide for clinicians regarding available therapies and a reference for researchers in this field.
tumour. Clinical and histopathological data were collected prospectively and analysed retrospectively. Seven patients were treated by a transperitoneal approach and two patients had a retroperitoneal approach. RESULTS: Relapse occurred within a mean time of 83 months (7-168) following nephrectomy. Recurrent tumour size varied from 2.5 to 4.5 cm. All surgeries were performed laparoscopically without need for conversion. Mean operative duration was 144 min (40-240), mean estimated blood loss was 430 mL (50-1300) and mean hospital stay was 4.5 days (3-6). Three patients had Clavien grade I intraoperative complications. Late complications were noted in two patients (Clavien I and IIIb). Pathology confirmed clear cell carcinoma in all patients with an absence of sarcomatoid features and negative surgical margins. Three patients had neoadjuvant treatment and two patients had adjuvant treatment. In all, 67% of patients were disease free with a mean follow-up period of 3 years. CONCLUSIONS: Surgical removal of isolated local recurrence remains the only possibility of cure in patients with renal cell carcinoma. We demonstrated that the laparoscopic approach is a safe and feasible alternative treatment option for selected cases with low morbidity and satisfactory oncological outcomes.

[397]

**TITULO / TITLE:** Aptamer-conjugated and doxorubicin-loaded unimolecular micelles for targeted therapy of prostate cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Xu W; Siddiqui IA; Nihal M; Pilla S; Rosenthal K; Mukhtar H; Gong S

**INSTITUCIÓN / INSTITUTION:** Department of Biomedical Engineering and Wisconsin Institutes for Discovery, University of Wisconsin-Madison, Madison, WI 53715, USA.

**RESUMEN / SUMMARY:** In the absence of effective therapy for prostate cancer, there is an immense need for developing improved therapeutic options for the management of this disease. This study has demonstrated that aptamer-conjugated unimolecular micelles can improve the in vivo tumor biodistribution of systemically administered anti-cancer drugs in prostate cancer expressing prostate-specific membrane antigen (PSMA). The aptamer-conjugated unimolecular micelles were formed by individual hyperbranched polymer molecules consisting of a hyperbranched H40 polymer core and approximately 25 amphiphilic polylactide-poly(ethlyene glycol) (PLA-PEG) block copolymer arms (H40-PLA-PEG-Apt). The unimolecular micelles with an average hydrodynamic diameter of 69 nm exhibited a pH-sensitive and controlled drug
release behavior. The targeted unimolecular micelles (i.e., DOX-loaded H40-PLA-PEG-Apt) exhibited a much higher cellular uptake in PSMA positive CWR22Rnu1 prostate carcinoma cells than non-targeted unimolecular micelles (i.e., DOX-loaded H40-PLA-PEG), thereby leading to a significantly higher cytotoxicity. The DOX-loaded unimolecular micelles up-regulated the cleavage of PARP and Caspase 3 proteins and increased the protein expression of Bax along with a concomitant decrease in Bcl2. These micelles also increased the protein expression of cell cycle regulation marker P21 and P27. In CWR22Rnu1 tumor-bearing mice, DOX-loaded H40-PLA-PEG-Apt micelles (i.e., targeted) also exhibited a much higher level of DOX accumulation in the tumor tissue than DOX-loaded H40-PLA-PEG micelles (i.e., non-targeted). These findings suggest that aptamer-conjugated unimolecular micelles may potentially be an effective drug nanocarrier to effectively treat prostate cancer.
TMPRSS2-ERG-positive prostate cancer cells may help to identify novel molecular targets and pathways for personalized therapy.

[399]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Farioli A; Violante FS; Mattioli S; Curti S; Kriebel D
INSTITUCIÓN / INSTITUTION: - Section of Occupational Medicine, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy.
PURPOSE: To investigate the association between external beam radiotherapy (EBRT) for prostate cancer and mesothelioma using data from the US Surveillance, Epidemiology, and End Results (SEER) cancer registries. METHODS: We analyzed data from the SEER database (1973-2009). We compared EBRT versus no radiotherapy. Incidence rate ratios (IRR) and 95 % confidence intervals (95 % CI) of mesothelioma among prostate cancer patients were estimated with multilevel Poisson models adjusted by race, age, and calendar year. Confounding by asbestos was investigated using relative risk of mesothelioma in each case’s county of residence as a proxy for asbestos exposure. RESULTS: Four hundred and seventy-one mesothelioma cases (93.6 % pleural) occurred in 3,985,991 person-years. The IRR of mesothelioma was increased for subjects exposed to EBRT (1.28; 95 % CI 1.05, 1.55) compared to non-irradiated patients, and a population attributable fraction of 0.49 % (95 % CI 0.11, 0.81) was estimated. The IRR increased with latency period: 0-4 years, IRR 1.08 (95 % CI 0.81, 1.44); 5-9 years, IRR 1.31 (95 % CI 0.93, 1.85); >/=10 years, IRR 1.59 (95 % CI 1.05, 2.42). Despite the fairly strong evidence of association with EBRT, the population attributable rate of mesothelioma was modest-3.3 cases per 100,000 person-years. The cumulative incidence of mesothelioma attributable to EBRT was 4.0/100,000 over 5 years, 24.5/100,000 over 10 years, and 65.0/100,000 over 15 years. CONCLUSIONS: Our study provides evidence that EBRT for prostate cancer is a small but detectable risk factor for mesothelioma. Patients should be advised of risk of radiation-induced second malignancies.

[400]
TÍTULO / TITLE: - Risk factors for acute kidney injury after radical nephrectomy and inferior vena cava thrombectomy for renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
**OBJECTIVE:** The objectives of the present study are to estimate the incidence of postoperative acute kidney injury (AKI) after radical nephrectomy with inferior vena cava (IVC) thrombectomy for renal cell carcinoma (RCC) based on the Acute Kidney Injury Network (AKIN) criteria, to investigate the risk factors for postoperative AKI, and to define the association between postoperative AKI and clinical outcome in patients undergoing such a surgery. **METHODS:** We retrospectively analyzed 76 patients (22 women; mean age, 56.9 years; range, 29-83 years) with RCC and IVC thrombus who underwent radical nephrectomy and IVC thrombectomy at our institute between January 2003 and December 2011. Postoperative AKI was diagnosed after surgery based on the AKIN criteria. Logistic regression was used to model the association between preoperative factors and the risk of AKI after surgery. The relationship between postoperative AKI and clinical outcomes, including chronic kidney disease (CKD), mortality, and days in hospital, was investigated. **RESULTS:** Postoperative AKI was diagnosed in 41 patients (53.9%) based on the AKIN criteria (stage 1, n = 34; stage 2, n = 2; and stage 3, n = 5). Multivariate analysis demonstrated an independent association between postoperative AKI and male gender (odds ratio 4.79, 95% confidence interval: 1.13-20.39; P = .034), and IVC clamping time lasting more than 20 minutes (odds ratio 6.60, 95% confidence interval: 1.48-29.42; P = .013). Development of AKI was associated with an increased rate of postoperative CKD (43.9% vs 20.0%; P = .031) and prolonged hospitalization (17.7 vs 12.2 days; P = .047). Only one patient who had postoperative AKI required renal replacement therapy. There was no 30-day mortality during the study period and no difference in mortality between AKI and non-AKI patients (4.9% vs 5.7%; P = .859). **CONCLUSIONS:** The incidence of postoperative AKI in patients with RCC and IVC thrombus was considerable. Intraoperative management seems to influence the risk of AKI after surgery; particularly, the longer the IVC clamping time, the higher the risk of postoperative AKI. Postoperative AKI was associated with postoperative CKD (P = .031), prolonged hospitalization (P = .047), and increased long-term mortality (1 year after surgery).
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-1145

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[402]

- CASTELLANO -

TÍTULO / TITLE: Costo beneficio de la detección de células prostáticas circulantes como test de tamizaje para cancer de próstata.

TÍTULO / TITLE: - Cost-Benefit of incorporating the detection of circulating prostate cells in a screening programme for prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Murray NP; Reyes E; Orellana N; Tapia P

RESUMEN / SUMMARY: - OBJECTIVES: Prostate cancer is the second most common cancer in men after skin cancer, screening is used to detect early stage cancer using serum prostate specific antigen(PSA). A level of PSA 4.0ng/ml as a cut-off point or abnormal digital rectal examination (DRE) are used to indicate a prostate biopsy. Nevertheless, non-malignant pathologies can increase serum PSA level so that 70% of biopsies are negative for cancer, and thus potentially unnecessary, causing anxiety, costly clinical tests and prolonged follow-up. Thus the search for new biomarkers is important. Circulating primary prostate cells (CPCs) may be such a marker. We analyze a cohort of patients using CPCs to detect prostate cancer in men with a serum PSA 4.0ng/ml or abnormal DRE in terms of cost-benefit. METHODS: A cohort of 263 patients with a PSA 4.0 ng/ml and a test to detect CPCs who underwent prostate biopsy were analyzed. The results of both tests were compared with biopsy results; sensibility, specificity, and predictive values were calculated. Costs of each test, process, drug costs and complications were determined as well as indirect costs. RESULTS: Of the 263 patients, 77 (28.6%) had prostate cancer detected, for the test using CPCs there was a sensibility of 85.7%, specificity of 90.3% and negative predictive value of 93.9%. Thus men CPC negative may not need a prostate biopsy. Potential savings for the 263 patients were between euro32,068 in a public health service and euro69,253 for inpatient private health insurance patients. Follow up cost were higher in false-positive CPC patients but, as there were fewer false positive patients, total costs were lower. CONCLUSIONS: The use of primary CPC detection as a complementary test in men with a serum PSA 4.0ng/ml to indicate prostate...
biopsy is a specific, cost effective test, eliminating approximately 70% of prostate biopsies. This results in a significant health care saving both in direct and indirect costs, in the costs of complications. Implementation costs were minimal as equipment and reagents are part of the routine clinical laboratory. The method deserves further investigation to confirm the results.

[403]
TÍTULO / TITLE: - The prevalence and prognostic significance of KRAS mutation in bladder cancer, chronic myeloid leukemia and colorectal cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1007/s11033-013-2512-8
AUTORES / AUTHORS: - Ouerhani S; Bougatef K; Soltani I; Elgaiaied AB; Abbes S; Menif S
INSTITUCION / INSTITUTION: - Laboratory of Molecular and Cellular Haematology, Pasteur Institute of Tunis, University of Tunis El Manar, Tunis, Tunisia, slah_mekni@yahoo.fr.
RESUMEN / SUMMARY: - Mutations in the KRAS gene have been shown to play a key role in the pathogenesis of a variety of human tumours. However the mutational spectrum of KRAS gene differs by organ site. In this study, we have analysed the mutational spectrum of KRAS exon 1 in bladder tumours, colorectal cancer (CRC) and chronic myeloid leukemia (CML). A total of 366 patients were included in the present study (234 bladder tumours, 48 CRC and 84 CML). The KRAS mutations are absent in BCR/ABL1 positive CML. This result suggests that BCR/ABL1 fusion gene and KRAS mutations were mutually exclusive. The frequency of KRAS mutations in bladder cancer was estimated at 4.27 %. All of mutations were found in codon 12 and 90 % of them were detected in advanced bladder tumours. However the correlation between KRAS mutations and tumour stage and grade does not report a statistical significant association. The KRAS mutations occur in 35.41 % of patients with CRC. The most frequent mutations were G12C, G12D and G13D. These mutations were significantly correlated with histological differentiation of CRC (p = 0.024). Although the high frequency of KRAS in CRC in comparison to bladder cancer, these two cancers appear to have the same mutational spectrum (p > 0.05).

[404]
TÍTULO / TITLE: - Prognostic value of PTEN loss in men with conservatively managed localised prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Background: The natural history of prostate cancer is highly variable and difficult to predict. We report on the prognostic value of phosphatase and tensin homologue (PTEN) loss in a cohort of 675 men with conservatively managed prostate cancer diagnosed by transurethral resection of the prostate. Methods: The PTEN status was assayed by immunohistochemistry (PTEN IHC) and fluorescent in situ hybridisation (PTEN FISH). The primary end point was death from prostate cancer. Results: The PTEN IHC loss was observed in 18% cases. This was significantly associated with prostate cancer death in univariate analysis (hazard ratio (HR)=3.51; 95% CI 2.60-4.73; \(P=3.1 \times 10^{-14}\)). It was highly predictive of prostate cancer death in the 50% of patients with a low risk score based on Gleason score, PSA, Ki-67 and extent of disease (HR=7.4; 95% CI 2.2-24.6; \(P=0.012\)), but had no prognostic value in the higher risk patients. The PTEN FISH loss was only weakly associated with PTEN IHC loss (kappa=0.5). Both PTEN FISH loss and amplification were univariately predictive of death from prostate cancer, but this was not maintained in the multivariate analyses. Conclusion: In low-risk patients, PTEN IHC loss adds prognostic value to Gleason score, PSA, Ki-67 and extent of disease.
candidates for active surveillance. MATERIALS AND METHODS: In a prospectively-collected institutional database, we identified 7,486 subjects eligible for active surveillance who underwent radical retropubic prostatectomy. Candidates were designated as low-risk (LR; stage T1c/T2a, PSA \( \leq 10 \) ng/ml, and Gleason score \( \leq 6 \)) or very low-risk (VLR; stage T1c, PSA density \( \leq 0.15 \), Gleason score \( \leq 6 \), \( \leq 2 \) positive biopsy cores, \( \leq 50\% \) cancer involvement per core) based on pre-operative data. Adverse findings were Gleason score upgrade (GS\( \leq 7 \)) and non organ-confined cancer (NOCC) on surgical pathology. The relative risk (RR) of adverse findings in men with LR and VLR disease were evaluated in a multivariable model using Poisson regression. RESULTS: 7,333 subjects met criteria for LR disease and 153 had VLR disease. The proportions of LR subjects found to have GS upgrade or non organ-confined cancer (NOCC) on final pathology were 21.8% and 23.1%, respectively. The corresponding values in VLR subjects were 13.1% and 8.5%. After adjusting for age, race, year of surgery, BMI, and PSA at diagnosis, the relative risk of GS upgrade in LR versus VLR disease was 1.89 (95% CI: 1.21-2.95). Relative risk of NOCC was 2.06 (95% CI: 1.19-3.57). CONCLUSION: Men with very low-risk prostate cancer had a significantly lower risk of adverse findings at surgery compared to those with low-risk disease. These data support the stratification of low risk cancer when selecting and counseling men who may be appropriate for active surveillance.

[406]
TITULO / TITLE: - The TERE1 (UBIAD1) bladder tumor suppressor protein interacts with mitochondrial TBL2: regulation of trans-membrane potential, oxidative stress and SXR signaling to the nucleus.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Fredericks WJ; McGarvey T; Wang H; Zheng Y; Fredericks NJ; Yin H; Wang LP; Hsiao W; Lee R; Weiss JS; Nickerson ML; Kruth HS; Rauscher FJ 3rd; Malkowicz SB
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Division of Urology, University of Pennsylvania and Veterans Affairs Medical Center Philadelphia, University and Woodland Ave., Research Building Room A418, Philadelphia, PA, 19104.
RESUMEN / SUMMARY: - We originally discovered TERE1 as a potential tumor suppressor protein based upon reduced expression in bladder and prostate cancer specimens and growth inhibition of tumor cell lines/xenografts upon ectopic expression. Analysis of TERE1 (aka UBIAD1) has shown it is a prenyltransferase enzyme in the natural bio-synthetic pathways for both vitamin K-2 and COQ10 production and exhibits multiple subcellular localizations
including mitochondria, endoplasmic reticulum, and golgi. Vitamin K-2 is involved in mitochondrial electron transport, SXR nuclear hormone receptor signaling and redox cycling: together these functions may form the basis for tumor suppressor function. To gain further insight into mechanisms of growth suppression and enzymatic regulation of TERE1 we isolated TERE1 associated proteins and identified the WD40 repeat, mitochondrial protein TBL2. We examined whether disease specific mutations in TERE1 affected interactions with TBL2 and the role of each protein in altering mitochondrial function, ROS/RNS production and SXR target gene regulation. Biochemical binding assays demonstrated a direct, high affinity interaction between TERE1 and TBL2 proteins; TERE1 was localized to both mitochondrial and non-mitochondrial membranes whereas TBL2 was predominantly mitochondrial; multiple independent single amino acid substitutions in TERE1 which cause a human hereditary corneal disease reduced binding to TBL2 strongly suggesting the relevance of this interaction. Ectopic TERE1 expression elevated mitochondrial trans-membrane potential, oxidative stress, NO production, and activated SXR targets. A TERE1-TBL2 complex likely functions in oxidative/nitrosative stress, lipid metabolism, and SXR signaling pathways in its role as a tumor suppressor. J. Cell. Biochem. © 2013 Wiley Periodicals, Inc.

[407]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Zhang G; Wang T; Gao L; Quan D

INSTITUCIÓN / INSTITUTION: - Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing 100850, China.

RESUMEN / SUMMARY: - LXT-101, a cationic peptide is a novel antagonist of gonadotropin-releasing hormone (GnRH) for prostate cancer treatment. However, effective delivery of peptide drugs into the body by the oral route remains a major challenge due to their origin properties with high molecular weights, strong polarity and low stability in the gastrointestinal (GI) tract. In this study, we have developed a novel oral delivery of oil-based formulation in which therapeutic peptide LXT-101 are solubilized in oils and with this solution as oil phase, an optimum formulation of self-microemulsifying drug delivery system (SMEDDS) was developed. The peptide stability with the SMEDDS formulation in artificial gastric and intestinal fluid was tested in vitro. On the
other hand, the testosterone level and plasma concentration of LXT-101 in rats after oral administration of the SMEDDS formulation were investigated in vivo. The data in vitro indicated that LXT-101 in the SMEDDS formulation was stable over 8h in artificial gastric and intestinal fluid. LXT-101 can be absorbed in vivo and suppression of testosterone maintained in castration level within 12h can be achieved effectively after SMEDDS formulation administered orally at a dose of 3.5mg/kg. The approach can provide a potential way for delivery peptides by oral.

[408]

**TÍTULO / TITLE:** - Overexpression of the chromatin remodeler death-domain-associated protein in prostate cancer is an independent predictor of early prostate-specific antigen recurrence.

**RESUMEN / SUMMARY:** - Molecular markers reliably predicting the aggressiveness of prostate cancer are currently lacking. Death-domain-associated protein (DAXX) has been implicated in the regulation of chromatin remodeling, transcription, and apoptosis that are integral to oncogenesis and cancer progression. DAXX expression was analyzed by immunohistochemistry on a tissue microarray containing 7478 prostate cancer specimens. Results were compared with tumor phenotype, biochemical recurrence, and v-ets erythroblastosis virus E26 oncogene homolog (ERG) status. DAXX expression was predominantly seen in the nucleus. DAXX expression was detectable in 4609 (80.6%) of 5718 interpretable cancers and considered strong in 5.9%, moderate in 45.8%, and weak in 28.9%. Strong DAXX expression was associated with both transmembrane protease, serine 2 (TMPRSS2)/ERG rearrangement and ERG expression (P < .0001 each). Strong DAXX expression was tightly linked to high Gleason grade, advanced pT stage, increased cell proliferation index, and early prostate-specific antigen recurrence (P < .0001 each). The prognostic role of DAXX expression was independent of Gleason grade, pT stage, and pN stage. Our study establishes DAXX as a novel independent prognosticator in prostate cancer and suggests an important role of DAXX expression for both prostate cancer development and progression.
Furthermore, DAXX appears to exert biologically different effects in ERG-positive and ERG-negative prostate cancers.

[409]

**TÍTULO / TITLE:** Molecular interplay between cdk4 and p21 dictates G/G cell cycle arrest in prostate cancer cells.

**RESUMEN / SUMMARY:** This study examined the effect of 3, 9-dihydroxy-2-prenylcoumestan (pso), a furanocoumarin, on PC-3 and C4-2B castration-resistant prostate cancer (CRPC) cell lines. Pso caused significant G0/G1 cell cycle arrest and inhibition of cell growth. Molecular analysis of cyclin (D1, D2, D3, and E), cyclin-dependent kinase (cdk) (cdks 2, 4, and 6), and cdk inhibitor (p21 and p27) expression suggested transcriptional regulation of the cdk inhibitors and more significant downregulation of cdk4 than of cyclins or other cdk5. Overexpression of cdk4, or silencing of p21 or p27, overcame pso-induced G0/G1 arrest, suggesting that G0/G1 cell cycle arrest is a potential mechanism of growth inhibition in CRPC cells.

[410]

**TÍTULO / TITLE:** Age-period-cohort Analysis of Renal Cell Carcinoma in United States Adults.

**RESUMEN / SUMMARY:** This study examined the effect of 3, 9-dihydroxy-2-prenylcoumestan (pso), a furanocoumarin, on PC-3 and C4-2B castration-resistant prostate cancer (CRPC) cell lines. Pso caused significant G0/G1 cell cycle arrest and inhibition of cell growth. Molecular analysis of cyclin (D1, D2, D3, and E), cyclin-dependent kinase (cdk) (cdks 2, 4, and 6), and cdk inhibitor (p21 and p27) expression suggested transcriptional regulation of the cdk inhibitors and more significant downregulation of cdk4 than of cyclins or other cdk5. Overexpression of cdk4, or silencing of p21 or p27, overcame pso-induced G0/G1 arrest, suggesting that G0/G1 cell cycle arrest is a potential mechanism of growth inhibition in CRPC cells.
of kidney cancer in the United States. METHODS: Cancer registry data from the National Cancer Institute’s Surveillance, Epidemiology, and End-Results (SEER) program were obtained for 64,041 patients with kidney cancer diagnosed between 1973 and 2008. Overall and age-specific incidence rates were calculated and adjustments were made for birth cohort and period effects. Results were stratified by race and sex. Age-period-cohort analysis was used to examine the effects of age, year of diagnosis (period), and year of birth (cohort) on incidence trends. RESULTS: The overall age-standardized annual incidence per 100,000 increased during the study period (1973 to 2008) by race, from 6.75 (95% confidence interval, 6.18-7.36) to 19.56 (18.85-20.20) among whites, from 5.31 (3.50-7.71) to 25.38 (23.00-27.92) among blacks, and from 5.61 (3.50-8.50) to 13.98 (12.41-15.71) among other races; and by sex, from 9.44 (8.49-10.47) to 26.48 (25.39-27.60) among men and from 4.21 (3.65-4.84) to 13.38 (12.64-14.11) among women. Age-period-cohort analysis revealed a strong influence from period and cohort effects. The 1983 birth cohort, for example, had a 2-fold increase in kidney cancer (incidence rate ratio, 1.93 [1.63-2.25]) compared with the referent 1948 cohort. CONCLUSION: From 1973 to 2008, the incidence rate of kidney cancer increased for each sex and race across all age groups. Age-period-cohort models revealed that period-related factors, although significant, cannot alone account for these unfavorable temporal trends.

[411]

TÍTULO / TITLE: - Comparative validation of nomograms predicting clinically insignificant prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Iremashvili V; Soloway MS; Pelaez L; Rosenberg DL; Manoharan M
INSTITUCIÓN / INSTITUTION: - Department of Urology, Miller School of Medicine, University of Miami, Miami, FL. Electronic address: viremashvili@med.miami.edu.
RESUMEN / SUMMARY: - OBJECTIVE: To validate and compare the accuracy and performance of nomograms predicting insignificant prostate cancer and to analyze their performance in patients with different cancer locations.
METHODS: Our cohort consisted of 370 radical prostatectomy patients with Gleason <=6 prostate cancer diagnosed on transrectal biopsy with at least 10 cores. We quantified the performance of each nomogram with respect to discrimination, calibration, predictive accuracy at different cut points, and the
clinical net benefit. We also evaluated these parameters in subgroups of patients with predominantly anterior-apical (AA) and posterior-basal (PB) tumor location. RESULTS: Insignificant prostate cancer was present in 141 patients (38%). The Kattan and Steyerberg nomograms outperformed other studied models and demonstrated fair discrimination (areas under the receiver operating characteristics curve 0.768 and 0.770, respectively), good calibration, balanced predictive accuracy, and the highest net benefit. All nomograms were less accurate at higher levels of predicted probability. The performance of the nomograms was better in patients with PB tumors than in those with AA tumors. The loss of correlation with the actual prevalence of insignificant prostate cancer at higher levels of predicted probability was not seen in the PB subgroup but was particularly noticeable in the AA subgroup. CONCLUSION: The Kattan and Steyerberg nomograms demonstrated the best performance in predicting the probability of insignificant prostate cancer in a contemporary cohort of patients with Gleason ≤ 6 cancer diagnosed on specimens from an extended transrectal biopsy. However, all studied nomograms were more accurate in identifying significant rather than insignificant disease, particularly for tumors located in the apical and anterior prostate.
of p27 protein levels was due to more gene transcription and an increase in protein stability. The increased stability of p27 was induced by delocalisation of Skp2 and a lower level of p27 phosphorylation at Thr187. AKT1 and AKT2 ablation inhibited and stimulated PC-3 cell migration, respectively. An AKT isoform-specific function could be associated with its subcellular localization. We found that AKT1 and AKT2 were mainly localised in the cytoplasm and nucleus, respectively. In androgen-sensitive cell line LNCaP, the ablation of AKT1 or AKT2 caused apoptosis but in androgen-independent LNCaP sublines, the effect of AKT1 ablation was lower; whereas no changes were observed after AKT2 ablation. Taken together, our data show that AKT1 and AKT2 have non-redundant roles in the regulation of PC-3 cell proliferation and migration. These could be explained by their subcellular localization and/or the specific regulation of downstream effectors. Furthermore, contribution of AKT isoforms to the progression of prostate cancer may change from an androgen-sensitive to a hormone-refractory stage. These findings may help design new targeted strategies for inhibiting AKT isoforms in prostate cancer.
staining, comet assay, DAPI staining and DNA gel electrophoresis showed that ellagic acid induced apoptosis and DNA damage in TSGH8301 cells. Western blotting assay showed that ellagic acid promoted p21, p53 and decreased CDC2 and WEE1 for leading to G0/G1 phase arrest and promoting BAD expression, AIF and Endo G, cytochrome c, caspase-9 and -3 for leading to apoptosis in TSGH8301 cells. On the basis of these observations, we suggest that ellagic acid induced cytotoxic effects for causing a decrease in the percentage of viable cells via G0/G1 phase arrest and induction of apoptosis in TSGH8301 cells. © 2013 Wiley Periodicals, Inc. Environ Toxicol, 2013.

[414]

TITULO / TITLE: A novel role of ribonuclease inhibitor in regulation of epithelial-to-mesenchymal transition and ILK signaling pathway in bladder cancer cells.

RESUMEN / SUMMARY: Human ribonuclease inhibitor (RI) is a cytoplasmic acidic protein possibly involved in biological functions other than the inhibition of RNase A and angiogenin activities. We have previously shown that RI can inhibit growth and metastasis in some cancer cells. Epithelial-mesenchymal transition (EMT) is regarded as the beginning of invasion and metastasis and has been implicated in the metastasis of bladder cancer. We therefore postulate that RI regulates EMT of bladder cancer cells. We find that the over-expression of RI induces the up-regulation of E-cadherin, accompanied with the decreased expression of proteins associated with EMT, such as N-cadherin, Snail, Slug, vimentin and Twist and of matrix metalloprotein-2 (MMP-2), MMP-9 and Cyclin-D1, both in vitro and in vivo. The up-regulation of RI inhibits cell proliferation, migration and invasion, alters cell morphology and adhesion and leads to the rearrangement of the cytoskeleton in vitro. We also demonstrate that the up-regulation of RI can decrease the expression of integrin-linked kinase (ILK), a central component of signaling cascades controlling an array of biological processes. The over-expression of RI reduces the phosphorylation of the ILK downstream signaling targets p-Akt and p-GSK3beta in T24 cells. We further find that bladder cancer with a high-metastasis capability shows higher vimentin, Snail, Slug and Twist and lower E-cadherin and RI expression in human clinical specimens. Finally, we provide evidence that the up-regulation of RI inhibits tumorigenesis and metastasis of bladder cancer in vivo. Thus, RI
might play a novel role in the development of bladder cancer through regulating EMT and the ILK signaling pathway.

[415]

**Título / Title:** Molecular Pathways: Fumarate Hydratase-Deficient Kidney Cancer: Targeting the Warburg Effect in Cancer.

**Resumen / Summary:** Hereditary leiomyomatosis and renal cell carcinoma (HLRCC) is a hereditary cancer syndrome in which affected individuals are at risk for development of cutaneous and uterine leiomyomas and an aggressive form of type II papillary kidney cancer. HLRCC is characterized by germline mutation of the tricarboxylic acid cycle (TCA) enzyme, fumarate hydratase (FH). FH-deficient kidney cancer is characterized by impaired oxidative phosphorylation and a metabolic shift to aerobic glycolysis, a form of metabolic reprogramming known as the Warburg effect. Increased glycolysis generates ATP needed for increased cell proliferation. Levels of the cellular energy sensor, AMPK, are decreased in FH-deficient kidney cancer; resulting in diminished p53 levels and decreased expression of the iron importer, DMT1, leading to low cellular iron levels and enhanced fatty acid synthesis by diminishing phosphorylation of acetyl CoA carboxylase, a rate limiting step for fatty acid synthesis. Increased fumarate and decreased iron levels in FH-deficient kidney cancer cells inactivate prolyl hydroxylases, leading to stabilization of HIF1alpha, and increased expression of genes such as vascular endothelial growth factor (VEGF) and GLUT1 to provide fuel needed for rapid growth demands. Therapeutic approaches for targeting the metabolic basis of FH-deficient kidney cancer are under development or are being evaluated in clinical trials. These same types of metabolic shifts have been found in a wide variety of other cancer types. Targeting the metabolic basis of a rare cancer such as FH-deficient kidney cancer will hopefully provide the foundation for the development of effective forms of therapies for other, more common cancers.

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[416]

**Título / Title:** Still not enough evidence to support screening based on prostate specific antigen.

**Resumen / Summary:**
miR-154 inhibits EMT by targeting HMGA2 in prostate cancer cells.

Epithelial-mesenchymal transition (EMT) is a crucial process that plays an important role in the invasion and metastasis of human cancers. High-mobility group AT-hook 2 (HMGA2) has been found to be involved in the EMT program, with its aberrant expression having been observed in a variety of malignant tumors. However, the mechanisms regulating HMGA2 expression remain incompletely understood. The objective of this study was to investigate whether mir-154 plays a critical role in EMT by regulating HMGA2. The expression levels of HMGA2 were examined in four samples of prostate cancer (PCa) tissue and adjacent non-tumorous tissue by Western blot analysis. The effects of forced expression of miR-154 or HMGA2 knockdown on PCa cells were evaluated by cell migration and invasion assays and Western blot analysis. HMGA2 was upregulated in the PCa tissue samples compared with the adjacent normal ones. Forced expression of miR-154 or HMGA2 knockdown significantly reduced the migratory and invasive capabilities of PCa cells in vitro and inhibited EMT gene expression, increased the levels of E-cadherin, an epithelial marker, and decreased the levels of vimentin, a mesenchymal marker. HMGA2 is a direct target gene of miR-154 by dual-luciferase reporter assay. Our findings suggest that miR-154 plays a role in regulating EMT by targeting HMGA2. Understanding the targets and regulating pathways of miR-154 may provide new insights into the underlying pathogenesis of PCa.
**Título / Title:** High diagnostic ability of multi-parametric magnetic resonance imaging in detecting anterior prostate cancer missed by transrectal 12-core biopsy.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary


**Autores / Authors:** Komai Y; Numao N; Yoshida S; Matsuoka Y; Nakanishi Y; Ishii C; Koga F; Saito K; Masuda H; Fujii Y; Kawakami S; Kihara K

**Institución / Institution:** Department of Urology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan.

**Resumen / Summary:** Purposo: We aimed to clarify the diagnostic ability of multiparametric magnetic resonance imaging (MP-MRI) to reveal anterior cancers missed by transrectal 12-core prostate biopsy (TR12PBx), based on the results of three-dimensional 26-core prostate biopsy (3D26PBx), a combination of TR12PBx and transperineal 14-core biopsy (TP14PBx) procedures. MATERIALS AND METHODS: The study population consisted of 324 patients who prospectively underwent prebiopsy MP-MRI and then 3D26PBx at a single institution. We defined TR12-negative cancer as cancer detected by TP14PBx but not by TR12PBx. We focused on cancers located in the anterior region. Any suspicious findings for malignancy in the region anterior to the urethra on MP-MRI were defined as anterior lesion on MP-MRI. Significant cancer was defined as biopsy GS >/= 4+3 and/or percent positive core > 20% and/or maximum cancer length >/= 5mm. The associations between anterior lesion on MP-MRI and TR12-negative cancer were investigated. RESULTS: The overall cancer detection rate by 3D26PBx was 39% (128/324), and of these 28% (36/128) were TR12-negative cancers. Anterior lesion on prebiopsy MP-MRI was identified in 20% (65/324) of the overall cohort. Of men with or without anterior lesion on MP-MRI, 40% (26/65) or 3.8% (10/259) had a TR12-negative cancer, respectively. Significant TR12-negative cancer was observed in 0.4% (1/259) of men without anterior lesion on MP-MRI. Prebiopsy MP-MRI presented anterior lesion in 92% (11/12) of significant TR12-negative cancers. CONCLUSIONS: Prebiopsy MP-MRI has a potential to efficiently select men who could have advantages by anterior samplings in addition to TR12PBx.

[419]

**Título / Title:** The Relationship Between the Site of Metastases and Outcome in Children With Stage IV Wilms Tumor: Data From 3 European Pediatric Cancer Institutions.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary

El objetivo de este estudio fue analizar con detenimiento el sitio de metástasis del WT de fase 4 y su correlación con el resultado. Las bases de datos de 3 instituciones europeas de cáncer pediátrico de mayor importancia se revisaron para niños con WT entre 1994 y 2011. De 208 niños identificados, 31 (14.9%) tuvieron metástasis al diagnóstico. El pulmón fue afectado en 29 niños (93.5%) y el hígado en 6 niños (19.4%). Veintisiete niños (87.1%) tuvieron metástasis aisladas a un órgano, siendo el pulmón el sitio más común (80.7%). El 5-year overall survival fue significativamente mejor en aquellos niños con enfermedad a distancia en pulmón o hígado (95.8%) comparado con aquellos afectados en ambos pulmón y hígado (57.1%, P=0.028). Además, los marcadores pronósticos fueron la respuesta de las metástasis a la quimioterapia preoperatoria (P=0.0138), histología de alto riesgo (P=0.024), y la etapa local (P=0.026). El 5-year overall survival fue de 82.1% y el 5-year event-free survival de 67.9%. El tiempo de seguimiento total fue de 74.1 y 87.2 (2 a 151) meses entre supervivientes, y la tasa de complicaciones relacionadas con el tratamiento fue del 16.7%. En conclusión, en nuestra serie de WT de fase 4, el pronóstico fue excelente si la histología era favorable, la enfermedad metastásica estaba aislada en pulmón o hígado, y si las metástasis respondieron a la quimioterapia preoperatoria.
RESUMEN / SUMMARY: - CONTEXT: Despite the effectiveness of bacillus Calmette-Guerin (BCG) therapy in non-muscle-invasive bladder cancer (NIMBC) to delay recurrence and disease progression, the evidence supporting maintenance treatment and its optimal duration is unknown. OBJECTIVE: The purposes of this paper are to critically review the evidence supporting the use of maintenance BCG after an initial series of induction instillations and to illustrate the factors contributing to current dilemmas in establishing the optimal duration of BCG treatment. EVIDENCE ACQUISITION: The following terms were used in Medline database searches for original articles published before February 1, 2013: bladder cancer, urothelial cancer, bacillus Calmette-Guerin, maintenance, and induction. All randomized controlled trials and meta-analyses, including those based on indirect comparisons, were evaluated. EVIDENCE SYNTHESIS: Seven randomized studies compared induction BCG plus maintenance to induction alone, with or without retreatment with BCG on recurrence. All but one of these studies were underpowered and the largest study used a broad, composite end point: worsening-free survival. Seven meta-analyses have been conducted, three of which included data from observational cohort studies. They demonstrated the benefit of maintenance BCG to reduce disease recurrence and delay progression compared to various control groups; however, the analyses were based on suboptimal data. Although there is new evidence that 1 yr of maintenance BCG is sufficient treatment in intermediate-risk patients, the optimal duration of BCG maintenance remains unknown. A new randomized trial is proposed, which includes induction BCG with retreatment on recurrence as a control arm, to study this question. CONCLUSIONS: The optimal duration of BCG treatment in patients with NMIBC remains unknown and should be the subject of further studies. We recommend that in addition to 3 yr of maintenance BCG, guideline panels also include 1 yr of therapy and induction BCG with retreatment on recurrence as a possible treatment options for patients with NMIBC, albeit with a lower level of evidence and grade of recommendation.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.02.3216
AUTORES / AUTHORS: - Taneja SS
TÍTULO / TITLE: - Quercetin synergizes with 2-methoxyestradiol inhibiting cell growth and inducing apoptosis in human prostate cancer cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wang G; Song L; Wang H; Xing N
INSTITUCIÓN / INSTITUTION: - Department of Urology, Beijing Chaoyang Hospital, Capital Medical University, Beijing 100020, P.R. China.
RESUMEN / SUMMARY: - Lack of effective treatment options for castration-resistant prostate cancer reinforces the great need to develop novel drug therapies. Quercetin is a plant-derived flavonoid that can induce apoptosis in prostate cancer cells. 2-Methoxyestradiol (2-ME) is an endogenous estrogenic metabolite that also has antineoplastic activity. However, these two agents have limited bioavailability. Herein, we explored the antiproliferative and proapoptotic activities of quercetin combined with 2-ME in both androgen-dependent LNCaP and androgen-independent PC-3 human prostate cancer cell lines. Compared to quercetin and 2-ME alone, combining quercetin with 2-ME at appropriate concentrations i) showed synergistic antiproliferative and proapoptotic activities; ii) increased G2/M phase population of cells; iii) decreased the ratio of Bcl-2/Bax significantly. The combination of quercetin and 2-ME is a new clinically relevant treatment regimen which has the potential of enhancing the antitumor effect on prostate cancer and lessening the side effect of either quercetin or 2-ME alone.

TÍTULO / TITLE: - Active extracts of black tea (Camellia Sinensis) induce apoptosis of PC-3 prostate cancer cells via mitochondrial dysfunction.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Sun S; Pan S; Miao A; Ling C; Pang S; Tang J; Chen D; Zhao C
INSTITUCIÓN / INSTITUTION: - Drink Plant Research Institute/Tea Research Center, Guangdong Academy of Agricultural Sciences, Guangzhou, Guangdong 510640, P.R. China.
RESUMEN / SUMMARY: - Cancer of the prostate gland is the most common invasive malignancy and the second leading cause of cancer-related death in human males. Many studies have shown that black tea reduces the risk of several types of cancer. We studied the effects of active extracts of black tea
and the black tea polyphenols theaflavins (TFs), on the cellular proliferation and mitochondria of the human prostate cancer cell line PC-3. Our studies revealed that Yinghong black tea extracts (YBT), Assam black tea extracts (ABT) and TFs inhibited cell proliferation in a dose-dependent manner. We also showed that TFs, YBT and ABT affected the morphology of PC-3 cells and induced apoptosis or even necrosis in PC-3 cells. In addition, it was observed that the samples significantly caused loss of the mitochondrial membrane potential, release of cytochrome c from the intermembrane space into the cytosol, decrease of the ATP content and activation of caspase-3 compared with the control. Taken together, these findings suggest that black tea could act as an effective anti-proliferative agent in PC-3 cells, and TFs, YBT and ABT induced apoptosis of PC-3 cells through mitochondrial dysfunction.
Multivariate analyses determined that sex, Fuhrman grade, pT stage 2010 and histological subtype were independent prognostic factors of disease-free survival, while sex, Fuhrman grade, pT stage 2010, M stage 2010, histological subtype and microvascular invasion were prognostic factors for cancer-specific survival. CONCLUSIONS: Our study shows that microvascular tumor invasion is an independent prognostic factor for cancer-specific survival in surgically treated patients with renal cell carcinoma.
Pancreatic secretory trypsin inhibitor causes autocrine-mediated migration & invasion in bladder cancer & phosphorylates the EGF receptor, Akt 2 & 3, ERK1 & 2.

Pancreatic secretory trypsin inhibitor is expressed in most bladder carcinomas where its pathophysiological relevance is unclear. Using recombinant normal sequence PSTI/TATI, a variant associated with familial pancreatitis (N34S), an active site inactivated variant (R18/V19) and immunoneutralization and RNA interference-mediated knockdown (KD) techniques, we investigated the actions of PSTI/TATI on cell migration (wounding monolayers), collagen invasion (gel invasion assays) and proliferation (Alamar blue) on 253J, RT4 and HT1376 human bladder carcinoma cell lines. All three forms of PSTI/TATI stimulated migration two-fold and normal sequence PSTI/TATI showed synergistic promigratory effects when added with EGF. Addition of structurally unrelated soya bean trypsin inhibitor had no promigratory activity. Similar results were seen using collagen invasion assays although the active site mutated variant had no pro-invasive activity, probably due to reduced Akt2 activation. PSTI/TATI did not stimulate proliferation despite acting, at least partially, through the EGF receptor as effects of PSTI/TATI were truncated by adding an EGFR blocking antibody or the tyrosine kinase inhibitor Tyrphostin. Cell lines produced endogenous PSTI/TATI and PSTI/TATI RNA interference knockdown or addition of PSTI/TATI, EGF-receptor or Tyrphostin blocking agents reduced migration and invasion below baseline. PSTI/TATI induced phosphorylation of the EGF receptor, ERK1 and 2, Akt2 and 3, JNK1, MKK3 and RSK1. This profile was more limited than that induced by EGF and did not include Akt1, probably explaining lack of pro-proliferative activity. Our findings of autocrine stimulation and synergistic responses between EGF & PSTI/TATI at concentrations found in urine and tissue suggest PSTI/TATI has pathophysiological relevance.

The expression of IL-6 and STAT3 might predict progression and unfavorable prognosis in Wilms' tumor.
PURPOSE: To investigate the expression profiles of IL-6 and STAT3 in Wilms’ tumor (WT) and their relationship with disease progression. METHODS: Immunohistochemistry was used to examine IL-6 and STAT3 expression in 58 primary tumors and 18 invasive/metastatic ones. RESULTS: Positive expression rate of IL-6/STAT3 was 39.7% (23/58)/29.3% (17/58) in primary WT tissues, while 61.1% (11/18)/33.3% (6/18) in associated invasive/metastatic tissues. The expression rate of IL-6 and STAT3 was higher in primary WT tumors of invasive/metastatic group than that of non-invasive/metastatic group (P=0.033; P=0.012). There was a positive correlation between IL-6 and STAT3 expression in 76 WT tissues (P<0.001, r=0.444). The expression of IL-6/STAT3 between primary WT and matched invasive/metastatic tissues was concordance (P=0.727; P=0.99). IL-6 expression status and histopathological type were associated with disease-free survival (DFS) and overall survival (OS) (P<0.05), while STAT3 was only correlated with DFS (P<0.05). CONCLUSIONS: IL-6 and STAT3 expression in WT might be correlated with progression and predict unfavorable prognosis, highlighting a new therapy target for invasive or metastatic WTs.
RESUMEN / SUMMARY: - BACKGROUND: Treatment decisions can be difficult in men with low-risk prostate cancer (PCa). OBJECTIVE: To evaluate the ability of a panel of four kallikrein markers in blood-total prostate-specific antigen (PSA), free PSA, intact PSA, and kallikrein-related peptidase 2-to distinguish between pathologically insignificant and aggressive disease on pathologic examination of radical prostatectomy (RP) specimens as well as to calculate the number of avoidable surgeries. DESIGN, SETTING, AND PARTICIPANTS: The cohort comprised 392 screened men participating in rounds 1 and 2 of the Rotterdam arm of the European Randomized Study of Screening for Prostate Cancer. Patients were diagnosed with PCa because of an elevated PSA \( \geq 3.0 \) ng/ml and were treated with RP between 1994 and 2004. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: We calculated the accuracy (area under the curve [AUC]) of statistical models to predict pathologically aggressive PCa (pT3-T4, extracapsular extension, tumor volume >0.5cm3, or any Gleason grade \( \geq 4 \)) based on clinical predictors (age, stage, PSA, biopsy findings) with and without levels of four kallikrein markers in blood. RESULTS AND LIMITATIONS: A total of 261 patients (67%) had significant disease on pathologic evaluation of the RP specimen. While the clinical model had good accuracy in predicting aggressive disease, reflected in a corrected AUC of 0.81, the four kallikrein markers enhanced the base model, with an AUC of 0.84 (\( p < 0.0005 \)). The model retained its ability in patients with low-risk and very-low-risk disease and in comparison with the Steyerberg nomogram, a published prediction model. Clinical application of the model incorporating the kallikrein markers would reduce rates of surgery by 135 of 1000 patients overall and 110 of 334 patients with pathologically insignificant disease. A limitation of the present study is that clinicians may be hesitant to make recommendations against active treatment on the basis of a statistical model. CONCLUSIONS: Our study provided proof of principle that predictions based on levels of four kallikrein markers in blood distinguish between pathologically insignificant and aggressive disease after RP with good accuracy. In the future, clinical use of the model could potentially reduce rates of immediate unnecessary active treatment.

[429]

TÍTULO / TITLE: - Effect of a novel bladder preservation therapy, BOAI-CDDP-radiation (OMC-regimen).
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Enlace al texto completo (gratuito o de pago) 3892/ijo.2013.1923
We have developed a novel form of bladder preservation therapy [OMC (Osaka Medical College)-regimen] involving balloon-occluded-arterial-infusion (BOAI) of an anticancer agent (cisplatin/gemcitabine), used concomitantly with hemodialysis, which delivers an extremely high concentration of anticancer agent to the site of a tumor without systemic adverse effects, along with concurrent radiation. We previously reported that the OMC-regimen elicited a complete response (CR) in >90% of patients with organ confined tumors, while LN(+), T4 tumors and a non-UC histological type were statistically significant risk factors for treatment failure and patient survival. In this study, we investigated the effects of the OMC-regimen in patients with organ confined urothelial cancer tumors and the outcomes were compared to those with total cystectomy. Three hundred and one patients were assigned to receive either the OMC-regimen (n=162) or total cystectomy (n=139). Patients in the OMC-regimen group who failed to achieve CR underwent cystectomy, or secondary BOAI with an increased amount of CDDP or gemcitabine (1600 mg). The OMC-regimen yielded 98.1% of clinical response; CR in 93.8% (152/162) of patients; PR in 4.3% (7/162). More than 96% of the CR patients (146/152) were alive with no evidence of recurrence after a mean follow-up of 166 (range 23-960) weeks. No patients suffered grade III toxicity; all patients successfully completed this therapy. The patient survival was significantly better compared to the cystectomy group; the overall 5-, 10- and 15-year survival rates were 87.3, 79.6 and 59.7%, respectively. Moreover, the 5-, 10- and 15-year bladder intact survival rates, the most important issue for bladder preservation therapy, were 85.7, 78.4 and 58.8%, respectively. In conclusion, the OMC-regimen is a useful bladder-preservation strategy, not only in those for whom cystectomy is indicated, but also in patients whose condition is not amenable to curative treatment and for whom palliation would otherwise seem the only option.
**AUTORES / AUTHORS:** - Saarelainen SK; Peltonen N; Lehtimaki T; Perheentupa A; Vuento MH; Maenpaa JU

**INSTITUCIÓN / INSTITUTION:** - Department of Obstetrics and Gynecology, Tampere University Hospital, Tampere, Finland. Electronic address: sami.saarelainen@uta.fi.

**RESUMEN / SUMMARY:** - OBJECTIVE: The purpose of this study was to evaluate the performance of preoperative serum levels of human epididymis protein 4 (HE4) and cancer antigen 125 (CA125) in the prediction of the presence of metastases in endometrial carcinoma. STUDY DESIGN: Preoperative sera were collected from 98 women with a diagnosis of endometrial carcinoma. The concentrations of HE4 and CA125 were assessed by enzyme-linked immunosorbent assay and correlated with the results of the final histopathologic report. RESULTS: Fourteen patients had metastases (≥stage IIIA, International Federation of Gynecology and Obstetrics 2009 classification). The serum concentrations of HE4 and CA125 were higher in the group with metastases than in the group without metastases (median [interquartile range], 148.6 pmol/L [71.6-219.1 pmol/L] vs 77.2 pmol/L [52.9-99.3 pmol/L]; P = .001; and 20.0 U/mL [10.1-70.8 U/mL] vs 4.3 U/mL [2.9-10.4 U/mL]; P < .001, respectively). By a multivariate analysis, the combination of HE4 and CA125 (a risk score algorithm) was the only predictive factor for the presence of metastases (odds ratio, 21.562; 95% confidence interval, 5.472-84.963; P < .001), and the grade was the predictor for a deep (≥50%) myometrial invasion by the tumor (odds ratio, 2.005; 95% confidence interval, 1.123-3.581; P = .019). The sensitivity, specificity, positive predictive value, and negative predictive value for the combination of the markers to predict the presence of metastases were 71.4%, 89.5%, 55.6%, and 94.4%, respectively. CONCLUSION: A combination of preoperative HE4 and CA125 seems to be a better predictor of metastatic disease than either 1 alone in endometrial carcinoma.

[431]

**TÍTULO / TITLE:** - CCR2 and CCR5 genes polymorphisms in benign prostatic hyperplasia and prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago)
1016/j.humimm.2013.04.031

**AUTORES / AUTHORS:** - Zambra FM; Biolchi V; Brum IS; Chies JA

**INSTITUCIÓN / INSTITUTION:** - Department of Genetics, Instituto de Biociencias, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil. Electronic address: fbzamba@gmail.com.
RESUMEN / SUMMARY: - Benign prostatic hyperplasia (BPH) and prostate cancer (PCa) are two chronic conditions, very common in aged men, that have been associated to inflammatory process. Chemokines and their receptors are recognized as critical mediators of inflammatory responses, they regulate immune cell migration and are implicated in tumor pathogenesis. The impact of two chemokine receptor gene polymorphisms, CCR2-64I (rs1799864) and CCR5-Delta32 (rs333), was evaluated in BPH and PCa. 385 DNA samples (130 BPH, 136 PCa, 119 healthy control) were genotyped. The allele frequencies were similar among control, BPH and PCa groups. Median of serum PSA levels was different between groups: 0.79, 1.45 and 6.91ng/mL in control, BPH and PCa groups, respectively (all p<0.001). The prostate volume median was 20.00cm3 in the control group, thus, lower than BPH (35.35cm3) and PCa (35.80cm3) (both p<0.001), nevertheless no statistical significant difference was observed between BPH and PCa patients (p=0.172). Remarkably, CCR2-64I was a protective factor to PCa when compared with BPH (OR=0.550; 95%CI=0.311-0.975), although the statistically significant difference was lost after correction for multiple comparisons. No significant associations of CCR5-Delta32 variant were observed with BPH, PCa or PCa clinicopathologic status. Our data suggest the influence of CCR2-64I variant in the development of prostate cancer.

[432]

TÍTULO / TITLE: - Toll-like receptor 9 agonist IMO cooperates with everolimus in renal cell carcinoma by interfering with tumour growth and angiogenesis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Damiano V; Rosa R; Formisano L; Nappi L; Gelardi T; Marciano R; Cozzolino I; Troncone G; Agrawal S; Veneziani BM; De Placido S; Bianco R; Tortora G


RESUMEN / SUMMARY: - Background:Targeting the mammalian target of rapamycin by everolimus is a successful approach for renal cell carcinoma (RCC) therapy. The Toll-like receptor 9 agonist immune modulatory oligonucleotide (IMO) exhibits direct antitumour and antiangiogenic activity and cooperates with both epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF) inhibitors.Methods:We tested the combination of IMO and everolimus on models of human RCC with different Von-Hippel Lindau (VHL) gene status, both in vitro and in nude mice. We studied their direct antiangiogenic effects on human umbilical vein endothelial
cells. Results: Both IMO and everolimus inhibited in vitro growth and survival of RCC cell lines, and their combination produced a synergistic inhibitory effect. Moreover, everolimus plus IMO interfered with EGFR-dependent signaling and reduced VEGF secretion in both VHL wild-type and mutant cells. In RCC tumour xenografts, IMO plus everolimus caused a potent and long-lasting cooperative antitumour activity, with reduction of tumour growth, prolongation of mice survival and inhibition of signal transduction. Furthermore, IMO and everolimus impaired the main endothelial cell functions. Conclusion: A combined treatment with everolimus and IMO is effective in VHL wild-type and mutant models of RCC by interfering with tumour growth and angiogenesis, thus representing a potentially effective, rationale-based combination to be translated in the clinical setting.

[433]
TÍTULO / TITLE: - MR-CT registration using a Ni-Ti prostate stent in image-guided radiotherapy of prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Korsager AS; Carl J; Ostergaard LR
INSTITUCIÓN / INSTITUTION: - Department of Health Science and Technology, Aalborg University, Aalborg 9220, Denmark.
RESUMEN / SUMMARY: - Purpose: In image-guided radiotherapy of prostate cancer defining the clinical target volume often relies on magnetic resonance (MR). The task of transferring the clinical target volume from MR to standard planning computed tomography (CT) is not trivial due to prostate mobility. In this paper, an automatic local registration approach is proposed based on a newly developed removable Ni-Ti prostate stent. Methods: The registration uses the voxel similarity measure of mutual information in a two-step approach where the pelvic bones are used to establish an initial registration for the local registration. Results: In a phantom study, the accuracy was measured to 0.97 mm and visual inspection showed accurate registration of all 30 data sets. The consistency of the registration was examined where translation and rotation displacements yield a rotation error of 0.41 degrees +/- 0.45 degrees and a translation error of 1.67 +/- 2.24 mm. Conclusions: This study demonstrated the feasibility for an automatic local MR-CT registration using the prostate stent.

[434]
TÍTULO / TITLE: - Expression of MMP-1, MMP-9 and TIMP-2 in prostate carcinoma and their influence on prognosis and survival.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ozden F; Saygin C; Uzunaslan D; Onal B; Durak H; Aki H
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Istanbul University Cerrahpasa Medical School, 34098, Kocamustafapasa/Istanbul, Turkey, ferhatnay@yahoo.com.

PURPOSE: Matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) participate in tumorigenesis, and their association with disease outcome is highly controversial. The present study investigates the influence of MMP-1, MMP-9 and TIMP-2 on different clinicopathologic variables and disease-free survival (DFS) of patients with prostate carcinoma. METHODS: Hundred and forty-five cases are included in the study, and levels of MMP/TIMP expressions are assessed in three tissue compartments (i.e., tumor, stroma and normal glands) with immunohistochemistry. RESULTS: Matrix metalloproteinase-1 expression in tumor cells was associated with lower Gleason scores, pretreatment prostate-specific antigen levels and lower incidence of vascular, perineural and extracapsular invasions. Moreover, MMP-9 positivity and TIMP-2 expression in normal glands were correlated with lower Gleason patterns and early stage at presentation. Expression of MMP in tumor cells and the presence of TIMP-2 in normal glands were associated with better DFS. CONCLUSION: Variability of MMP/TIMP expressions from case to case makes it difficult to evaluate their impact on clinical outcome. However, these proteins might be new and promising targets for prostate cancer therapy in the future.

[435]

TÍTULO / TITLE: - Effects of pyridine analogs of curcumin on growth, apoptosis and NF-kappaB activity in prostate cancer PC-3 cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wei X; Zhou D; Wang H; Ding N; Cui XX; Wang H; Verano M; Zhang K; Conney AH; Zheng X; DU ZY
INSTITUCIÓN / INSTITUTION: - Department of Chemistry and Chemical Engineering, Guangzhou University, Guangzhou, PR China.

RESUMEN / SUMMARY: - Twelve pyridine analogs of curcumin were studied for their effects on growth and apoptosis in human prostate cancer PC-3 cells. The ability of these compounds to inhibit the transcriptional activity of nuclear factor-kappa B (NF-kappaB) and the level of phosphorylated extracellular signal-regulated kinases (phospho-ERK1/2) in PC-3 cells was also determined.
Treatment of PC-3 cells with the pyridine analogs of curcumin resulted in concentration-dependent growth inhibition and apoptosis stimulation. Only pyridine analogs of curcumin with a tetrahydrothiopyrane-4-one linker (FN compounds) exhibited a strong inhibitory effect on growth and a strong stimulatory effect on apoptosis at low concentrations (\( \leq 1 \mu M \)). Mechanistic studies showed that NF-kappaB transcripational activity in PC-3 cells was strongly inhibited by treatment with group FN compounds. Treatment of PC-3 cells with 1 \( \mu M \) FN1 resulted in a decrease of activated ERK1/2. Results from the present study indicate that FN compounds warrant further in vivo studies using suitable animal models of prostate cancer.

[436]

**TÍTULO / TITLE:** Soluble FGL2 induced by tumor necrosis factor-alpha and interferon-gamma in CD4 T cells through MAPK pathway in human renal allograft acute rejection.

**RESUMEN / SUMMARY:**
Enlace al Resumen / Link to its Summary


autor(es / author(s)): Zhao Z; Wang L; Yang C; Zhao T; Li L; Hu L; Wu D; Rong R; Xu M; Zhu T

**INSTITUCIÓN / INSTITUTION:** Department of Urology, Zhongshan Hospital, Fudan University, Shanghai, China; Shanghai Key Laboratory of Organ Transplantation, Shanghai, China.

**RESUMEN / SUMMARY:** BACKGROUND: Acute rejection (AR), initiated by alloreactive CD4+ T cells, hampers allograft survival. Soluble fibrinogen-like protein 2 (sFGL2) is a novel effector of CD4+ T cells. We previously found that serum sFGL2 significantly increased in renal allograft recipients with AR. In this study, sFGL2 secretion by CD4+ T cells and its mechanism were further explored both in vivo and in vitro. MATERIALS AND METHODS: Forty cases of living-related renal transplant recipients with biopsy-proven AR or stable renal function were collected and detected serum sFGL2, tumor necrosis factor (TNF)-alpha and interferon (IFN)-gamma, and peripheral CD4+ T cells. In vitro, the isolated human CD4+ T cells were stimulated by TNF-alpha or IFN-gamma. sFGL2 in the supernatant and mitogen-activated protein kinase (MAPK) proteins in the CD4+ T cells were investigated. Approval for this study was obtained from the Ethics Committee of Fudan University. RESULTS: sFGL2, TNF-alpha, IFN-gamma, and CD4+ T cells were significantly increased in the peripheral blood of renal allograft recipients with AR. Stimulation with 1000 U/mL TNF-alpha or 62.5 U/mL IFN-gamma for 48 h provided an optimal condition for CD4+ T cells to secrete sFGL2 in vitro. Phosphorylated (p-) c-Jun N-terminal kinase was remarkably upregulated in the activated CD4+ T cells,
whereas no significant changes were found in p-p38 MAPK or p-ERK1/2 expression. Furthermore, inhibition of c-Jun N-terminal kinase significantly reduced sFGL2 secretion by CD4+ T cells. CONCLUSIONS: sFGL2 secretion by CD4+ T cells can be induced with TNF-alpha and IFN-gamma stimulation through MAPK signaling in renal allograft AR. Our study suggests that sFGL2 is a potential mediator in the pathogenesis of allograft rejection.
effects on the clinical course of the patients, resulting in a higher rate of progression to chronic prostatitis.

[438] TÍTULO / TITLE: - Undescended testis: The underlying mechanisms and the effects on germ cells that cause infertility and cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago)
1016/j.jpedsurg.2013.02.001
AUTORES / AUTHORS: - Hutson JM
INSTITUCIÓN / INSTITUTION: - Urology Department, Royal Children’s Hospital, Melbourne, Australia; Douglas Stephens Surgical Research Group, Murdoch Childrens Research Institute, Melbourne, Australia; Department of Paediatrics, University of Melbourne, Melbourne, Australia. Electronic address: john.hutson@rch.org.au.
RESUMEN / SUMMARY: - Testicular descent is a complex morphological process that occurs in at least 2 stages, with different hormonal control. Insl3 controls the first step of gubernacular enlargement, although the abnormality long gubernacular cord in persistent Mullerian duct syndrome remains unexplained. Androgens control inguinoscrotal migration, which may be triggered by local signalling from the mammary line, and which requires the genitofemoral nerve. However, there is still much to learn about this phase, which when abnormal frequently leads to cryptorchidism. Orchidopexy is being recommended in the first year of age, because increasing research suggests that the stem cells for spermatogenesis form between 3 and 9 months, with surgery aiming to permit this normally, although this is not yet proven. Acquired cryptorchidism is now becoming accepted and is likely to be caused by inadequate elongation of the postnatal spermatic cord. It is not yet known whether orchidopexy is always needed, as this remains controversial.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1210/en.2012-2077
AUTORES / AUTHORS: - Masoodi KZ; Ramos Garcia R; Pascal LE; Wang Y; Ma HM; O'Malley K; Eisermann K; Shevrin DH; Nguyen HM; Vessella RL; Nelson JB; Parikh RA; Wang Z
Androgen deprivation therapy (ADT) is the standard treatment for patients with PSA progression after treatment for localized prostate cancer. An alternative to continuous ADT is intermittent ADT (IADT), which allows recovery of testosterone during off-cycles to stimulate regrowth and differentiation of the regressed prostate tumor. IADT offers patients a reduction in side effects associated with ADT, improved quality of life, and reduced cost with no difference in overall survival. Our previous studies showed that IADT coupled with 5alpha-reductase inhibitor, which blocks testosterone conversion to dihydrotestosterone (DHT) could prolong survival of animals bearing androgen-sensitive prostate tumors when off-cycle duration was fixed.

To further investigate this clinically relevant observation, we measured the time course of testosterone-induced regrowth of regressed LuCaP35 and LNCaP xenograft tumors in the presence or absence of a 5alpha-reductase inhibitor. 5alpha-reductase inhibitors suppressed the initial regrowth of regressed prostate tumors. However, tumors resumed growth and were no longer responsive to 5alpha-reductase inhibition several days after testosterone replacement. This finding was substantiated by BrdU and Ki67 staining of LuCaP35 tumors, which showed inhibition of prostate tumor cell proliferation by 5alpha-reductase inhibitor on day 2, but not day 14, after testosterone replacement. 5alpha-reductase inhibitors also suppressed testosterone-stimulated proliferation of LNCaP cells pre-cultured in androgen-free media, suggesting that blocking testosterone conversion to DHT can inhibit prostate tumor cell proliferation via an intracrine mechanism. These results suggest that short off-cycle coupled with 5alpha-reductase inhibition could maximize suppression of prostate tumor growth and thus, improve potential survival benefit achieved in combination with IADT.

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TÍTULO / TITLE: Trimethoxy-Resveratrol and Piceatannol Administered Orally Suppress and Inhibit Tumor Formation and Growth in Prostate Cancer Xenografts.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Dias SJ; Li K; Rimando AM; Dhar S; Mizuno CS; Penman AD; Levenson AS
INSTITUCIÓN / INSTITUTION: Cancer Institute, University of Mississippi Medical Center, Jackson, Mississippi.
RESUMEN / SUMMARY: BACKGROUND: Resveratrol (Res) is recognized as a promising cancer chemoprevention dietary polyphenol with antioxidative, anti-
inflammatory, and anticancer properties. However, the role of its analogues in prostate cancer (PCa) chemoprevention is unknown. METHODS: We synthesized several natural and synthetic analogues of Res and characterized their effects on PCa cells in vitro using a cell proliferation assay. A colony formation assay and in vitro validation of luciferase (Luc) activity was done for LNCaP-Luc cells that were consequently used for in vivo studies. The efficacy of Res, trimethoxy-resveratrol (3M-Res) and piceatannol (PIC) was studied in a subcutaneous (s.c.) model of PCa using oral gavage. Tumor progression was monitored by traditional caliper and bioluminescent imaging. The levels of cytokines in serum were examined by ELISA, and the levels of compounds in serum and tumor tissues were determined by gas chromatography-mass spectrometry. RESULTS: We examined the anti-proliferative activities of Res/analogues in three PCa cell lines. We further compared the chemopreventive effects of oral Res, 3M-Res, and PIC in LNCaP-Luc-xenografts. We found that 2 weeks pretreatment with the compounds diminished cell colonization, reduced tumor volume, and decreased tumor growth in the xenografts. Both 3M-Res and PIC demonstrated higher potency in inhibiting tumor progression compared to Res. Notably, 3M-Res was the most active in inhibiting cell proliferation and suppressing colony formation, and its accumulation in both serum and tumor tissues was the highest. CONCLUSIONS: Our findings offer strong pre-clinical evidence for the utilization of dietary stilbenes, particularly 3M-Res, as novel, potent, effective chemopreventive agents in PCa. Prostate 9999: XX-XX, 2013. © 2013 Wiley Periodicals, Inc.

[441]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Notohamiprodjo S; Djafarzadeh R; Rieth N; Hofstetter M; Jaeckel C; Nelson PJ
INSTITUCIÓN / INSTITUTION: - Medizinische Klinik und Poliklinik IV, Campus Innenstadt, Universitat Mu nchen, Arbeitsgruppe Klinische Biochemie, Schillerstrasse 42, D-80336, Munich , Deutschland.
RESUMEN / SUMMARY: - Tissue inhibitor of metalloproteinase 1 (TIMP-1) controls matrix metalloproteinase activity through 1:1 stoichiometric binding. Human TIMP-1 fused to a glycosylphosphatidylinositol(GPI) anchor (TIMP-1 - GPI) shifts the activity of TIMP-1 from the extracellular matrix to the cell surface. TIMP-1 - GPI treated renal cell carcinoma cells show increased apoptosis and reduced proliferation. Transcriptomic profiling and regulatory
pathway mapping were used to identify the potential mechanisms driving these effects. Significant changes in the DNA binding inhibitors, TGF- beta 1/SMAD and BMP pathways resulted from TIMP-1 - GPI treatment. These events were linked to reduced TGF- beta 1 signaling mediated by inhibition of proteolytic processing of latent TGF- beta 1 by TIMP-1 - GPI.

[442]

- CASTELLANO -

TÍTULO / TITLE: Analisis del desempeno de la presencia de celulas prostaticas malignas circulantes como factor predictivo para la deteccion de cancer de prostata en la primera, segunda y tercera biopsia prostatica.

TÍTULO / TITLE: - A performance analysis of the presence of malignant circulating prostate cells as a predictive factor for the detection of prostate cancer in the first, second and third prostate biopsy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Murray NP; Reyes E; Tapia P; Badinez L; Orellana N; Fuentealba C; Olivares R; Duenas R


RESUMEN / SUMMARY: - OBJECTIVES: Serum prostate specific antigen and digital rectal examination are the tests used as screening tests to detect prostate cancer. However, only approximately 30% of men with suspicion of cancer have it confirmed on prostate biopsy, and not all of these need treatment. Detection of circulating tumor cells in localized prostate cancer has given variable results, but it could be a useful complementary screening tool to detect prostate cancer in men with abnormal screening tests before the evaluation with prostate biopsy. This may be more so in subsequent biopsies where serum PSA has a decreased diagnostic yield. To evaluate the diagnostic yield of the detection of CPCs as a complementary PC screening test in a population fulfilling criteria for an initial, second and third prostate biopsy for suspicion of PC. METHODS: A prospective screening study of consecutive patients aged 45-80 years presenting to the urologist for PC screening. Inclusion criteria were PSA 4.0ng/ml, PSA velocity 0.35ng/ml/year and/or DRE suspicious for cancer. Patients fulfilling inclusion criteria had blood taken for CPC detection and then underwent 12-core transrectal prostate biopsy. Double immune-his-tochemical staining with anti-PSA and anti-P504S was used to detect CPCs. Both cytologist and pathologist were blinded to the results of the biopsy, CPC results and clinical details. The diagnostic yield of the presence or absence of CPC was evaluated; the prostate biopsy was classified as cancer or
no-cancer. RESULTS: 282 men participated, 83 undergoing a second and 38 a third biopsy, with a mean age of 66.2 +/- 8.9 years and a median serum PSA of 5.10ng/ml, 5.45ng/ml and 6.45ng/ml for first, second and third biopsies. Cancer was detected in 33.6%, 10.8% and 29.0% of first, second and third biopsies respectively, CPCs were detected in 36.9%, 21.7% and 36.8% of the patients. Sensibility, specificity and negative predictive value were 86%, 91% and 94% for the first biopsy, 89%, 87% and 99% for the second and 100%, 89% and 100% for third biopsy respectively. All the CPC determinations were interpretable. There were 11 false negative cases, all with small low grade tumors. Of the 29 men with a false positive CPC, 8/10 had cancer detected in the subsequent biopsy. CONCLUSIONS: The use of CPC detection could be useful as a complementary prostate cancer screening test, especially for excluding cancer, and including patients with indications for repeat biopsies. Men with a false positive CPC detection had a high risk of detecting cancer in the succeeding biopsy.

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[443]

TÍTULO / TITLE: - Catechol estrogens induce proliferation and malignant transformation in prostate epithelial cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Mosli HA; Tolba MF; Al-Abd AM; Abdel-Naim AB

INSTITUCIÓN / INSTITUTION: - Department of Urology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia.

RESUMEN / SUMMARY: - In the current study, the non-transformed prostatic epithelial cells (BPH-1) were exposed to the catechol estrogens (CE) 2-hydroxyestradiol (2-OHE2) or 4-hydroxyestradiol (4-OHE2), or the parent hormone 17-beta-estradiol (E2) at an equimolar concentration (1muM) for a period of 6 weeks. It was found that both 2-OHE2 and 4-OHE2 have more potent proliferation-enhancing effect than E2. Exposure to 2-OHE2, 4-OHE2 or E2 resulted in a significant increase in the protein abundance of cyclin D1 and c-myc. The treated cells exhibited a shift toward the proliferative phase as indicated by FACScan. BPH-1 cells treated with 4-OHE2 showed increased abundance of estrogen receptor-alpha (ERalpha) and its downstream IGF-1R. Reduced abundance of estrogen receptor-beta (ERbeta) and its downstream tumor suppressor FOXO-1 were observed in cells exposed to E2, 2-OHE2 and, to a greater extent, 4-OHE2. Comet assay revealed that CE, especially 4-OHE2, elicited significant genotoxic effects as compared to E2. 4-OHE2 showed greater ability to neoplastically transform BPH-1 cells as indicated by
increased colony forming capacity in soft agar and matrix invasion. In conclusion, in vitro exposure to CE could neoplastically transform human prostatic epithelial cells. Further, 4-OHE2 is more carcinogenic to prostate epithelial cells than the parent hormone E2.
proportional to the amount and duration of addiction. Drinking water contaminated with arsenic and chromium chlorination byproducts increases the risk of BC. High consumption of red meat and saturated fat may increase the risk, while high intake of fruits and vegetables decreases it. Patients treated with cyclophosphamide, ifosfamide and ionizing radiation have an increased risk of BC. Frequent and prolonged use of hair dyes and Schistosoma haematobium infestation increases the risk of BC. CONCLUSIONS: The reduction or the cessation of smoking decrease BC. The contaminant-free water consumption with the increase of vegetal foods favour BC prevention. Cancer survivors treated with cyclophosphamide, ifosfamide and radiation therapy should be monitored for early diagnosis of BC.

TÍTULO / TITLE: Factores de riesgo constitucionales y ocupacionales asociados al cáncer vesical.

TÍTULO / TITLE: Constitutional and occupational risk factors associated with bladder cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Ferris J; Garcia J; Berbel O; Ortega JA

INSTITUCIÓN / INSTITUTION: Unitat de Salut Mediambiental Pediatrica, Unitat d'Oncologia Pediatrica, Hospital Universitari i Politecnic La Fe, Valencia, España. Electronic address: ferris_jos@gva.es.

RESUMEN / SUMMARY: OBJECTIVE: Bladder carcinoma (BC) is the fourth most common type of cancer in males from Western countries, with primary prevention an important healthcare challenge. We review the associated constitutional and occupational risk factors (RF), with greater or lesser scientific evidence, in the aetiology of BC. MATERIAL AND METHODS: Literature review of the last 25 years of the constitutional and occupational RF associated with BC, conducted on MedLine, CancerLit, Science Citation Index and Embase. The search profiles were Risk factors/Genetic factors/Genetic polymorphisms/Epidemiology/Occupational factors and Bladder cancer. RESULTS: The main RF were a) age and gender (diagnosed at age 65 and over, with a 4:1 ratio of males to females); b) race, ethnicity and geographic location (predominantly in Caucasians and in Southern European countries); c) genetic (N-acetyltransferase-2 and glutathione s-transferase M1 gene mutations, which significantly increase the risk for BC); d) occupational, which represent 5%-10% of BC RF; and f) occupations with high BC risk, such as
aluminium production, the manufacture of dyes, paints and colourings, the rubber industry and the extraction and industrial use of fossil fuels.

CONCLUSIONS: BC is the end result of the variable combination of constitutional and environmental RF, the majority of which are unknown. The most significant constitutional RF are related to age, gender, race, ethnicity geographic location and genetic polymorphisms. The main occupational RF are those related to aromatic amines and polycyclic aromatic hydrocarbons.

[447]

**TÍTULO / TITLE:** - TFE3 Break-apart FISH Has a Higher Sensitivity for Xp11.2 Translocation-associated Renal Cell Carcinoma Compared With TFE3 or Cathepsin K Immunohistochemical Staining Alone: Expanding the Morphologic Spectrum.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](1097/PAS.0b013e31827e17cb)


**AUTORES / AUTHORS:** - Rao Q; Williamson SR; Zhang S; Eble JN; Grignon DJ; Wang M; Zhou XJ; Huang W; Tan PH; Maclennan GT; Cheng L

**INSTITUCIÓN / INSTITUTION:** - *Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis, IN parallelDepartment of Pathology, Case Western Reserve University, Cleveland, OH daggerDepartment of Pathology, Nanjing Jinling Hospital, Nanjing University School of Medicine double daggerDepartment of Pathology, Nanjing Medical University Affiliated Nanjing Hospital (Nanjing First Hospital), Nanjing, China section signDepartment of Pathology, Singapore General Hospital, Singapore.

**RESUMEN / SUMMARY:** - Renal cell carcinoma (RCC) associated with Xp11.2 translocation is uncommon, characterized by several different translocations involving the TFE3 gene. We assessed the utility of break-apart fluorescence in situ hybridization (FISH) in establishing the diagnosis for suspected or unclassified cases with negative or equivocal TFE3 immunostaining by analyzing 24 renal cancers with break-apart TFE3 FISH and comparing the molecular findings with the results of TFE3 and cathepsin K immunostaining in the same tumors. Ten tumors were originally diagnosed as Xp11.2 RCC on the basis of positive TFE3 immunostaining, and 14 were originally considered unclassified RCCs with negative or equivocal TFE3 staining, but with a range of features suspicious for Xp11.2 RCC. Seventeen cases showed TFE3 rearrangement associated with Xp11.2 translocation by FISH, including all 13 tumors with moderate or strong TFE3 (n=10) or cathepsin K (n=7) immunoreactivity. FISH-positive cases showed negative or equivocal
immunoreactivity for TFE3 or cathepsin K in 7 and 10 tumors, respectively (both=3). None had positive immunohistochemistry but negative FISH. Morphologic features were typical for Xp11.2 RCC in 10/17 tumors. Unusual features included 1 melanotic Xp11.2 renal cancer, 1 tumor with mixed features of Xp11.2 RCC and clear cell RCC, and other tumors mimicking clear cell RCC, multilocular cystic RCC, or high-grade urothelial carcinoma. Morphology mimicking high-grade urothelial carcinoma has not been previously reported in these tumors. Psammoma bodies, hyalinized stroma, and intracellular pigment were preferentially identified in FISH-positive cases compared with FISH-negative cases. Our results support the clinical application of a TFE3 break-apart FISH assay for diagnosis and confirmation of Xp11.2 RCC and further expand the histopathologic spectrum of these neoplasms to include tumors with unusual features. A renal tumor with pathologic or clinical features highly suggestive of translocation-associated RCC but exhibiting negative or equivocal TFE3 immunostaining should be evaluated by TFE3 FISH assay to fully assess this possibility.

[448]
TÍTULO / TITLE: - Chromophobe renal cell carcinoma with sarcomatoid differentiation: a clinicopathologic study of 14 cases.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Lauer SR; Zhou M; Master VA; Osunkoya AO
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Emory University School of Medicine, Atlanta, GA 30322, USA.
RESUMEN / SUMMARY: - OBJECTIVE: To investigate the clinicopathologic features of chromophobe renal cell carcinoma with sarcomatoid differentiation. STUDY DESIGN: A search was made through the surgical pathology and expert consult files of two major academic institutions from 2003 to 2011 for cases of chromophobe renal cell carcinoma with sarcomatoid differentiation. RESULTS: Fourteen patients were identified. The patients included 9 males (64%) and 5 females (36%). The mean patient age was 60.4 years (range, 40-82 years). There was a left-sided predominance: left (9 patients) and right (5 patients). The mean tumor size was 14.6 cm (range, 9.5-28.0 cm), and the mean percentage sarcomatoid differentiation was 67% (range, 30-99%). All tumors exhibited moderate to extensive areas of necrosis. The nonsarcomatoid component in all cases demonstrated classic features of chromophobe renal cell carcinoma. Nine patients (64%) had pT3 disease and 5 patients (36%) had pT4 disease. Five patients (36%) had positive surgical margins. Three patients (21%) had tissue diagnosis of metastatic disease at the time of initial surgery. Six patients (43%) had subsequent pathologic and/or radiologic evidence of multiple or isolated metastatic disease. Follow-up information was available in
all 14 patients. Mean follow-up time was 16 weeks (range, 2-84 weeks). Ten of 14 patients (71%) died of disease, 9 of those within 6 months (mean survival time of 10 weeks), 3 patients (21%) were alive with disease, and only 1 patient (7%) was alive with no evidence of disease. CONCLUSION: This study is one of the largest series to date specifically examining the clinicopathologic features of sarcomatoid chromophobe renal cell carcinoma in radical nephrectomy specimens and confirms the observation that these tumors behave more aggressively than conventional clear cell renal cell carcinoma or papillary renal cell carcinoma.

[449]

TÍTULO / TITLE: - Increased expression of ALDH1A1 protein is associated with poor prognosis in clear cell renal cell carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Wang K; Chen X; Zhan Y; Jiang W; Liu X; Wang X; Wu B

INSTITUCIÓN / INSTITUTION: - Department of Urology, Sheng Jing Hospital of China Medical University, Shenyang 110004, Liaoning, People’s Republic of China.

RESUMEN / SUMMARY: - Aldehyde dehydrogenase 1α1 (ALDH1A1) has been characterized as a cancer stem cell marker in different types of tumors. It plays a key role in various biological processes in tumor, including cell proliferation, invasion and chemoresistance. Recently, ALDH1A1 has been described as a prognostic marker in various tumors. In this study, we detected the expression of ALDH1A1 in 95 clear cell renal cell carcinoma (ccRCC) by immunohistochemistry and correlated it with clinicopathological parameters and prognosis. We further explored the correlation of ALDH1A1 expression to proliferation, invasion and drug sensitivity of renal cancer cell in vitro by silencing of ALDH1A1 in A498 renal cell line. ALDH1A1 protein showed high expression in 53 of 95 cases of ccRCC (56.8%), which was significantly higher than that in normal tissues (5/23, 21.7%). ALDH1A1 overexpression was significantly associated with tumor stage (P = 0.000), recurrence (P = 0.000), tumor size (P = 0.000) and vascular invasion (P = 0.023). The Kaplan-Meier survival analysis demonstrated that ALDH1A1 overexpression was significantly associated with shorter recurrence-free survival and overall survival (P = 0.003 and P = 0.008, respectively). Multivariate analysis demonstrated that ALDH1A1 was an independent prognostic factor for patients with ccRCC. Experiments in vitro further showed ALDH1A1 played an essential role in proliferation, invasion
and drug sensitivity of renal cancer cell. In conclusion, ALDH1A1 might be a potential molecular marker in ccRCC, which provided us with a new therapeutic target in ccRCC.

[450] TÍTULO / TITLE: - Re: loss of the urothelial differentiation marker FOXA1 is associated with high grade, late stage bladder cancer and increased tumor proliferation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wood DP

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Le Broc-Ryckewaert D; Carpentier R; Lipka E; Daher S; Vaccher C; Betbeder D; Furman C
INSTITUCIÓN / INSTITUTION: - Universite Lille Nord de France, F-59000 Lille, France; UDSL, EA 4483, UFR Pharmacie, F-59000 Lille, France.
RESUMEN / SUMMARY: - Taxanes, including paclitaxel, are anti-cancer drugs approved for the treatment of prostate cancer but which have limited clinical application due to their hydrophobicity, their low therapeutic index and the emergence of chemoresistance. These side effects may be avoided through the use of new drug delivery systems such as nanoparticles, and paclitaxel-loaded PLGA nanoparticles up to 200nm in size have shown encouraging results. As it is known that size affects the tissular penetration and distribution of tumors via the enhanced permeability and retention effect, so nanoparticles smaller than 100nm are potentially interesting vehicles for improving paclitaxel delivery and efficacy. In this work, new paclitaxel-loaded small PLGA nanoparticles, between 49nm and 95nm in size and with positive or negative surface charges, were prepared without detergent. They were stable in the presence of serum, and HPLC showed that high paclitaxel loading and stability were achieved. Intracellular uptake of these nanoparticles was studied in PC3 cells by flow
Confocal studies confirmed a high tubulin destructuration at very low dose with these nanoparticles. This study suggests that both positively and negatively charged paclitaxel-loaded small PLGA nanoparticles deliver this drug into PC3 cells, and that this nanoparticle mode of delivery highly improves paclitaxel efficiency by up to two log-increase. These results also highlight the importance of small nanoparticles for drug delivery in cancer applications and are extremely promising for in vivo studies.

[452]

TÍTULO / TITLE: Association of prostate cancer susceptibility variant (MSMB) rs10993994 with risk of spermatogenic failure.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Wu W; Lu J; Yuan B; Qin Y; Chen M; Niu X; Xu B; Lu C; Xia Y; Chen D; Sha J; Wang X

INSTITUCIÓN / INSTITUTION: State Key Laboratory of Reproductive Medicine, Institute of Toxicology, Nanjing Medical University, Nanjing 210029, China; Key Laboratory of Modern Toxicology of Ministry of Education, School of Public Health, Nanjing Medical University, Nanjing 211166, China; Wuxi Maternal and Child Health Hospital Affiliated to Nanjing Medical University, Wuxi 214002, China. Electronic address: wwu@njmu.edu.cn.

RESUMEN / SUMMARY: beta-Microseminoprotein (MSMB) is one of the most abundant proteins in human seminal plasma. It has been identified that MSMB increased significantly in oligoasthenoteratozoospermic patients compared with fertile controls. We hypothesized that the functional polymorphism (rs10993994) of MSMB gene could be a risk factor for spermatogenic failure. For this study, 338 patients with idiopathic oligozoospermia or azoospermia and 382 fertile controls were recruited from an infertility clinic. Semen analysis was performed by computer-assisted semen analysis system. The functional polymorphism of MSMB gene was genotyped using TaqMan method. Sixty three seminal plasma samples were used to test the expression of MSMB by enzyme-linked immunosorbent assay (ELISA). The TT genotype and T allele were associated with an increased risk of idiopathic infertility with azoospermia (TT genotype: OR, 1.75; 95% CI, 1.03-2.95; T allele: OR, 1.34; 95% CI, 1.03-1.75). However, no differences were found in risk for the TT genotype or T allele among men with oligozoospermia. In addition, idiopathic infertile males have significantly higher MSMB expression levels than fertile controls. We present the first epidemiologic evidence supporting the involvement of common genetic polymorphism in MSMB gene in spermatogenic failure. These results suggest that men carrying the variant have an increased risk of spermatogenic failure.
associated with male infertility. Further studies are needed to confirm the roles of the polymorphism in idiopathic azoospermia and investigate the biological mechanism of elevated MSMB expression in infertile males.

[453]
**TÍTULO / TITLE:** - The role of functional imaging in the era of targeted therapy of renal cell carcinoma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - World J Urol. 2013 Apr 16.

**AUTORES / AUTHORS:** - Braunagel M; Graser A; Reiser M; Notohamiprodjo M

**INSTITUCIÓN / INSTITUTION:** - Department of Clinical Radiology, University Hospitals Munich, Campus Grosshadern, Marchioninistrasse 15, 81377, Munich, Germany, Margarita.Braunagel@med.uni-muenchen.de.

**RESUMEN / SUMMARY:** - Antiangiogenic therapies interacting with tumor-specific pathways have been established for targeted therapy of renal cell carcinoma (RCC). However, evaluation of tumor response based on morphologic tumor diameter measurements has limitations, as tumor shrinkage may lag behind pathophysiological response. Functional imaging techniques such as dynamic contrast-enhanced (DCE) ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI), unenhanced diffusion-weighted MRI (DW-MRI), and also metabolic imaging with positron emission tomography (PET) have the ability to assess physiological parameters and to predict and monitor therapy response. Assessment of changes in vascularity, cellularity, oxygenation, and glucose uptake with functional imaging during targeted therapy may correlate with progression-free survival and can predict tumor response or progression. In this review, we explore the potential of functional imaging techniques for assessing the effects of targeted therapy of RCC and as well review the reproducibility and limitations.

[454]
**TÍTULO / TITLE:** - Critical evaluation of MRI-targeted TRUS-guided transperineal fusion biopsy for detection of prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Kuru TH; Roethke MC; Seidenader J; Simpfendorfer T; Boxler S; Alammar K; Rieker P; Popeneiu VI; Roth W; Pahernik S; Schlemmer HP; Hohenfellner M; Hadaschik BA
INSTITUCIÓN / INSTITUTION: - Department of Urology, University Hospital Heidelberg, Heidelberg, Germany; Department of Radiology, German Cancer Research Center (DKFZ), Heidelberg, Germany. Electronic address: timur.kuru@med.uni-heidelberg.de.

RESUMEN / SUMMARY: - PURPOSE: Diagnosis and precise risk stratification of prostate cancer (PC) is essential for individualized treatment decisions. MRI/TRUS fusion has shown encouraging results for detecting clinically significant prostate cancer. Here we critically evaluate MRI-targeted TRUS-guided transperineal fusion biopsy in routine clinical practice. MATERIALS AND METHODS: 347 consecutive patients with suspicion of PC were prospectively included. The median age of patients was 65 years (range 42-84). Mean PSA level was 9.85ng/ml (0.5-104). 49% of men had previous negative TRUS-guided biopsies, 51% underwent primary biopsy. All patients underwent multiparametric (mp)-MRI at 3T and received systematic stereotactic prostate biopsies plus MRI-targeted TRUS-guided biopsies in case of MRI abnormalities. Imaging data and biopsy results were analyzed and a self-designed questionnaire was sent to all men regarding further clinical history and adverse effects of the biopsy. RESULTS: 200 of 347 (58%) biopsy samples showed PC. 73.5% of biopsy proven PC was clinically relevant (NCCN criteria). On mp-MRI, 104 men were reported as highly suspicious for PC and, in these, the tumor detection rate was 82.6% (86/104) with 72% Gleason scores >/=7. Overall, targeted cores detected significantly more cancer than systematic biopsies (30% vs. 8.2%). In patients without cancer-suspicious MRI-lesions, 11.7% (11/94) were diagnosed with intermediate risk disease. Regarding adverse effects, 50.6% of patients (152/300) reported mild hematuria, 26% temporary erectile dysfunction and 2.6% needed short-term catheterization after biopsy. In three patients (1%) non-septic febrile urinary tract infection occurred. CONCLUSIONS: MRI-targeted TRUS-guided transperineal fusion biopsy provides high detection rates of clinically significant tumors. mp-MRI still has some limitations, and therefore systematic biopsies should currently not be omitted. The morbidity of the transperineal saturation approach is reasonable and mainly self-limiting.

[455]

TÍTULO / TITLE: - Imaging-guided biopsy detects prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1002/cncr.28140

AUTORES / AUTHORS: - Printz C

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Cadmium in blood of Tunisian men and risk of bladder cancer: interactions with arsenic exposure and smoking.

RESUMEN / SUMMARY: Prior investigations identified an association between low-level blood arsenic (As) and bladder cancer risk among Tunisian men but questions remain regarding confounding by cadmium (Cd), a well-established bladder carcinogen. A case-control study of Tunisian men was re-examined to assess the levels of cadmium in blood and reparse the association between the simultaneous exposure to these metals and bladder cancer risk. Levels of blood Cd were significantly twice higher among cases than in controls (P < 0.05) and were positively correlated with smoking and age. Additionally, analysis of metal levels among non-smokers according to the region of residence showed very high blood Cd and As levels for the coastal regions of Sfax and central Tunisia. After controlling for potential confounders, for low blood As levels (<0.67 mug/L), the OR for blood Cd was 4.10 (95 % CI 1.64-10.81), while for higher levels (>0.67 mug/L), it was reduced to 2.10 (CI, 1.06-4.17). Adjustment for Cd exposure did not alter the risk associated to As exposure. This study is the first to report the relationship between Cd exposure and risk of bladder cancer occurrence in interaction with smoking and As exposure. Smoking is shown to be the main exposure source to Cd in the Tunisian population but also environmental pollution seems to be responsible for Cd exposure among non-smokers. Exposure assessment studies encompassing a wider population are needed.

Imaging treated prostate cancer.

RESUMEN / SUMMARY: Prior investigations identified an association between low-level blood arsenic (As) and bladder cancer risk among Tunisian men but questions remain regarding confounding by cadmium (Cd), a well-established bladder carcinogen. A case-control study of Tunisian men was re-examined to assess the levels of cadmium in blood and reparse the association between the simultaneous exposure to these metals and bladder cancer risk. Levels of blood Cd were significantly twice higher among cases than in controls (P < 0.05) and were positively correlated with smoking and age. Additionally, analysis of metal levels among non-smokers according to the region of residence showed very high blood Cd and As levels for the coastal regions of Sfax and central Tunisia. After controlling for potential confounders, for low blood As levels (<0.67 mug/L), the OR for blood Cd was 4.10 (95 % CI 1.64-10.81), while for higher levels (>0.67 mug/L), it was reduced to 2.10 (CI, 1.06-4.17). Adjustment for Cd exposure did not alter the risk associated to As exposure. This study is the first to report the relationship between Cd exposure and risk of bladder cancer occurrence in interaction with smoking and As exposure. Smoking is shown to be the main exposure source to Cd in the Tunisian population but also environmental pollution seems to be responsible for Cd exposure among non-smokers. Exposure assessment studies encompassing a wider population are needed.
RESUMEN / SUMMARY: In patients with a clinical suspicion of recurrence after treatment for prostate cancer, imaging can be used to distinguish between local recurrence and metastatic disease. Multiparametric magnetic resonance imaging (mpMRI) of the prostate may be a valuable imaging modality for the detection and localization of local recurrence in patients treated for prostate cancer. In mpMRI, morphological T2-weighted images are combined with functional MRI techniques including diffusion-weighted imaging, dynamic contrast-enhanced imaging, and magnetic resonance spectroscopic imaging to improve accuracy. In this paper, the current status of imaging techniques used to detect and to localize tumor recurrence in patients treated for prostate cancer will be reviewed, with emphasis on mpMRI for local prostate cancer recurrence.

TÍTULO / TITLE: Influence of survivin (BIRC5) and caspase-9 (CASP9) functional polymorphisms in renal cell carcinoma development: a study in a southern European population.

RESUMEN / SUMMARY: Renal cell carcinoma (RCC) is the most common cancer of the adult kidney and its incidence and mortality has increase in the last 20 years. The disruption of cellular death is one the mechanism involved in cancer development. This process is precise regulated by apoptotic and anti-apoptotic molecules. Survivin (BIRC5) is a member of the inhibitor of apoptosis protein family and has the ability to inhibit the activation of the pro-apoptotic caspase-9 (CASP9). Thus BIRC5 and CASP9 functional polymorphisms might modulate the apoptosis and consequently RCC development. Our purpose was to investigate the potential role of BIRC5-31G/C and CASP9+83C/T functional polymorphisms in the risk for the development of RCC and metastatic disease. We studied the BIRC5-31G/C and CASP9+83C/T functional polymorphisms by PCR-RFLP and allelic discrimination using the 7300 real-time polymerase chain reaction system, respectively, in 178 RCC patients and in 305 healthy controls.
individuals. Regarding the BIRC5-31G/C polymorphism, there is a trend to an overrepresentation of CC genotype in RCC group compared with normal controls (aOR, 1.94; P = 0.053). We observed, after gender stratification and age-adjustment, that BIRC5-31CC and CASP9+83CT/TT genotypes were associated with an increased risk for RCC development in the female group of our southern European study population (aOR = 3.85; P = 0.019; aOR = 2.98; P = 0.028; respectively). Concerning the waiting time for onset of metastatic disease, we observed that BIRC5-31CC homozygous developed metastasis 8 years earlier than the G carriers using a Cox proportional hazard model with gender as covariate (HR = 4.9, P = 0.038, P bootstrap = 0.009). The Cox regression proportional hazard model was validated using bootstrap statistic with 1,000 samples of the same number of patients as the original dataset. Our results suggest that individual differences influence the susceptibility to RCC and tumor behavior. This genetic profile may help to define higher risk groups that would benefit from individualized chemoprevention strategies and therapies.
factors or chemokines such as SDF-1, CXCR4, and VEGF. The possible role of PCa-MSCs in the process of PCa development needed further clarification.

[460]

**Título / Title:** Ring-substituted analogs of 3,3'-diindolylmethane (DIM) induce apoptosis and necrosis in androgen-dependent and -independent prostate cancer cells.

**Resumen / Summary:** We recently reported that novel ring-substituted analogs of 3,3'-diindolylmethane (ring-DIMs) have anti-androgenic and growth inhibitory effects in androgen-dependent prostate cancer cells. The objectives of this study were to confirm the ability of 4,4'- and 7,7'-dibromo- and dichloro-substituted ring-DIMs to inhibit androgen-stimulated proliferation of androgen-dependent LNCaP human prostate cancer cells using a non-invasive, real-time monitoring technique. In addition, their ability to induce apoptotic and necrotic cell death in androgen-dependent as well as -independent (PC-3) prostate cancer cells was studied. Prostate cancer cells were treated with increasing concentrations of DIM and ring-DIMs (0.3-30 μM) and effects on cell proliferation were measured in real-time using an xCELLigence cellular analysis system. Chromatin condensation and loss of membrane integrity were determined by Hoechst and propidium iodide staining, respectively. Apoptotic protein markers were measured by immunoblotting and activation of caspases determined using selective fluorogenic substrates. Intra- and extracellular concentrations of DIM and ring-DIMs were assessed by electrospray ionization tandem mass spectrometry. Ring-DIMs inhibited androgen-stimulated LNCaP cell proliferation and induced apoptosis and necrosis in LNCaP and PC-3 cells with 2-4 fold greater potencies than DIM. DIM and the ring-DIMs increased caspases -3, -8 and -9 activity, elevated expression of Fas, FasL, DR4 and DR5 protein, and induced PARP cleavage in both cell lines. The cytotoxicity of the most potent ring-DIM, 4,4'-dibromoDIM, but not the other compounds was decreased by an inhibitor of caspase -3. The 4,4'-dibromoDIM was primarily found in the extracellular medium, whereas all other compounds were present to a much larger extent in the cell. In conclusion, ring-DIMs inhibited prostate cancer cell growth and induced cell death in LNCaP and PC-3 cells with greater potencies than DIM; they also structure-dependently activated different cell
death pathways suggesting that these compounds have clinical potential as chemopreventive and chemotherapeutic agents in prostate cancer, regardless of hormone-dependency.

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RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - DEN Otter W; VAN Moorselaar RJ; Jacobs JJ; Haar RT; Koten JW; Dobrowolski Z; Lipczynski W; Pasukoniene V; Characiejus D; Jankevicius F; Eidukevicius R; DE Reijke TM
INSTITUCIÓN / INSTITUTION: - Department of Urology, Free University Medical Centre, Amsterdam, The Netherlands. W.denotter@vumc.nl.
RESUMEN / SUMMARY: - Aim: Comparison of the therapeutic effect of treatment of non-muscle invasive bladder carcinoma (NMIBC) after intravesical Interleukin-2 (IL-2) instillations in the presence and absence of a marker tumour. MATERIALS AND METHODS: Two pilot studies were performed in patients with NMIBC. The first study (10 patients) was performed in Krakow (Poland), the second (26 patients) in Vilnius (Lithuania). In Krakow the tumours were treated with incomplete transurethral resection (TUR) leaving a marker tumour of 0.5-1.0-cm followed by IL-2 instillations (3x10^6 IU IL-2) on five consecutive days. In Vilnius the tumours were treated with complete TUR, followed by IL-2 instillations (9x10^6 IU IL-2) on five consecutive days. RESULTS: During 30 months follow-up, the recurrence-free survival was 5/10 (50%) and 6/26 (23%) after incomplete and complete TUR, respectively. So, the ratio of the recurrence-free survival after incomplete/complete TUR of 50/23=2.2. The median of the recurrence-free survival is >20.5 months and 7 months after incomplete and complete TUR, respectively. So, this ratio was >20.5/7= >2.9. The hazard ratio which combines both the chance of the disease recurrence and its timing for both censored and uncensored cases was 0.53, again confirming the better outcome after incomplete TUR. CONCLUSION: A possible explanation for the better therapeutic effects after incomplete TUR compared with complete TUR is that the marker tumour has tumour-associated antigens (TAA) that could lead to an immune reaction that is stimulated by local application of IL-2. After complete TUR, no TAA are available to initiate and to stimulate an immune reaction; consequently, local IL-2 therapy is less effective after complete TUR. The results of these two pilot studies have led to the recent start of a randomised prospective clinical trial in which therapeutic effects of local IL-2 therapy after complete and incomplete TUR are compared.
In vitro and in vivo experimental models as tools to investigate the efficacy of antineoplastic drugs on urinary bladder cancer.

Several drugs have shown in vitro and in vivo pharmacological activity against urinary bladder cancer. This review aims at compiling the different drugs evaluated in in vitro and in vivo models of urinary bladder cancer and to review the advantages and limitations of both types of models, as well as the different methodologies applied for evaluating antineoplastic drug activity.
quintile adjusting for age. There was no association between SIMD quintile and prostate cancer deaths. CONCLUSION: Increased affluence was associated with higher likelihood of having a PSA test and a higher incidence of prostate cancer. However there were no observed differences by social class of the likelihood of having a positive PSA test or prostate cancer related death.

TÍTULO / TITLE: - Erythropoietin supports the survival of prostate cancer, but not growth and bone metastasis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Shiozawa Y; McGee S; Pienta MJ; McGregor N; Jung Y; Yumoto K; Wang J; Berry JE; Pienta KJ; Taichman RS
INSTITUCIÓN / INSTITUTION: - Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, 48109, USA.
RESUMEN / SUMMARY: - Erythropoietin (Epo) is used in clinical settings to enhance hematopoietic function and to improve the quality of life for patients undergoing chemotherapy by reducing fatigue and the need for transfusions. However, several meta-analyses have revealed that Epo treatments are associated with an increased risk of mortality in cancer patients. In this study, we examined the role of Epo in prostate cancer (PCa) progression, using in vitro cell culture systems and in vivo bone metastatic assays. We found that Epo did not stimulate the proliferation of PCa cell lines, but did protect PCa cells from apoptosis. In animal models of PCa metastasis, no evidence was found to support the hypothesis that Epo enhances metastasis. Together, these findings suggest that Epo may be useful for treating severe anemia in PCa patients without increasing metastatic risk. J. Cell. Biochem. © 2013 Wiley Periodicals, Inc.

TÍTULO / TITLE: - Significance of obesity markers and adipocytokines in high grade and high stage prostate cancer in North Indian men - A cross-sectional study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Tewari R; Rajender S; Natu SM; Goel A; Dalela D; Goel MM; Tondon P
INSTITUCIÓN / INSTITUTION: - Department of Pathology, King George Medical University, Lucknow, India; Department of Gastroenterology and Hepatology, Moti Lal Nehru Medical College (MLNMC), Allahabad, India. Electronic address: reshutewarikgmu@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: Prostate cancer (CaP) in India is the 10th most common malignancy affecting men. CaP incidence in India is low, but rising like other countries. The reasons for this racial disparity are uncertain. The foremost reasons that may underlie regional/ethnic differences are genetic polymorphisms, altered hormonal status, socioeconomic status, and obesity. This study aimed at investigating the role of adipocytokines in stimulating the promotion and progression of CaP. METHODS: A cross-sectional study on histopathologically proven prostate cancer (N=95) and benign prostatic hyperplasia (N=95) patients was undertaken. CaP patients were classified into high-grade (N=62) and low-grade (N=33), and high stage (N=31) and low stage (N=64) groups. The level of body mass index (BMI), waste to hip ratio (WHR), interleukin-6 (IL-6), leptin, and adiponectin were compared between BPH and CaP groups and between grades and stages of prostate cancer. RESULTS: The level of BMI was significantly (p<0.001) higher in CaP patients (26.58+/−4.76) in comparison to BPH (22.15+/−2.90). Similarly, WHR was significantly (p<0.0001) higher in the CaP patients (1.08+/−0.37) in comparison to BPH (0.86+/−0.15). Leptin (BPH: 25.60, CaP: 56.00) and IL-6 levels (BPH: 9.90, CaP: 32.30) were significantly higher, but adiponectin was significantly lower in CaP patients as compared to BPH. High grade CaP patients had significantly higher BMI and WHR in comparison to low grade, and WHR was also higher in high stage CaP. Leptin and IL-6 level were higher in high stage and high grade, but adiponectin was low in high stage and high grade groups in comparison to low stage and low grade groups. CONCLUSIONS: Higher BMI and WHR correlate with prostate cancer independently, suggesting obesity to be a promoter of poor prostate health. Leptin and IL-6 appear to have stimulating effect on prostate cancer cells inducing the promotion and progression of CaP, but adiponectin appears to be protective against prostate cancer.

TÍTULO / TITLE: - Ovarian Transitional Cell Carcinoma Represents a Poorly Differentiated Form of High-grade Serous or Endometrioid Adenocarcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Takeuchi T; Ohishi Y; Imamura H; Aman M; Shida K; Kobayashi H; Kato K; Oda Y
INSTITUCIÓN / INSTITUTION: - Departments of *Anatomic Pathology daggerHealth Sciences, Graduate School of Medical Sciences Kyushu University double daggerDepartment of Obstetrics and Gynecology, Kyushu University Hospital, Fukuoka, Japan.

RESUMEN / SUMMARIZED - Ovarian transitional cell tumors include Brenner tumors (BTs) and transitional cell carcinoma (TCC; non-BTs) according to the most recent World Health Organization classification. However, it remains a matter of debate whether TCC represents a distinct entity or a morphologic variant of high-grade serous adenocarcinoma (HG-SC). The purpose of this study was to resolve the above question by clarifying the morphologic, immunohistochemical, and molecular features of TCC. We reviewed 488 cases of epithelial ovarian carcinomas and reclassified them on the basis of the most recent World Health Organization classification with the modifications proposed by Kobel and colleagues, and 35 cases of TCC were identified; 25 and 6 TCCs were admixed with HG-SC and endometrioid adenocarcinoma (EC), respectively, and the remaining 4 cases were pure TCC. TCC components were not observed in any clear cell carcinomas or mucinous adenocarcinomas. Only 2 cases of malignant BT were identified. In addition to TCCs, malignant BTs, and related adenocarcinomas, benign and borderline BTs were included in the following immunohistochemical and molecular analyses. Immunohistochemically, pure TCCs, TCCs admixed with HG-SC, and pure HG-SCs were characterized by frequent aberrant p53 expression (diffuse or null pattern) and WT1/ER/PR/IMP2 immunophenotype, whereas BTs, including benign, borderline, and malignant BTs, were characterized by lack of aberrant p53 expression and WT1/ER/PR/IMP2 immunophenotype. In contrast to the BTs, pure ECs and TCCs admixed with EC showed an ER/PR immunophenotype. Nearly all the tumors with a TP53 gene mutation by molecular analysis showed aberrant p53 staining patterns. In conclusion, TCC is not a distinct entity but a poorly differentiated form of serous or EC, as (1) most TCCs coexist with HG-SC (mostly) or EC (occasionally), and (2) the immunophenotype and molecular features are similar to those of HG-SC or EC but different from those of BTs.

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TÍTULO / TITLE: - Decay of gamma-H2AX foci correlates with potentially lethal damage repair in prostate cancer cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - van Oorschot B; Hovingh SE; Rodermond H; Guclu A; Losekoot N; Geldof AA; Barendsen GW; Stalpers LJ; Franken NA
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Laboratory for Experimental Oncology and Radiobiology (LEXOR), Center for Experimental Molecular Medicine, Academic Medical Center, University of Amsterdam, and Free University Hospital, Amsterdam, The Netherlands.

RESUMEN / SUMMARY: - To determine the relationship between ionizing radiation-induced levels of gamma-H2AX foci and cell survival in cultured prostate cancer cell lines, three prostate cancer cell lines: LNCaP (wt TP53), DU145 (mut TP53) and PC3 (TP53 null), were studied. For gamma-H2AX foci induction, cells were irradiated with a single dose of 2 Gy and foci levels were studied at 30 min and 24 h after irradiation. Cell survival was determined by clonogenic assay, directly and 24 h after irradiation with doses ranging from 0 to 8 Gy. Irradiation was performed with a Siemens Stabilipan 250 KeV X-ray machine at a dose rate of approximately 3 Gy/min. Survival curves were analyzed using the linear-quadratic model \( S(D)/S(0) = \exp(-\alpha D + \beta D^2) \). LNCaP cells clearly demonstrated potentially lethal damage repair (PLDR) which was assessed as increased survival levels after delayed plating as compared to cells plated immediately after irradiation. DU145 cells demonstrated only a slight PLDR and PC3 cells did not show PLDR at all. Levels of gamma-H2AX foci were significantly decreased in all cell lines at 24 h after irradiation, compared to levels after 30 min. The LNCaP cells which demonstrated a clear PLDR also showed the largest decay in the number of gamma-H2AX foci. In addition, the PC cells which did not show PLDR had the lowest decay of gamma-H2AX foci. A clear correlation was demonstrated between the degree of decay of gamma-H2AX foci and PLDR.

TÍTULO / TITLE: - microRNA-330 inhibits cell motility by downregulating Sp1 in prostate cancer cells.

RESUMEN / SUMMARY: - microRNAs (miRNAs), small non-coding RNAs, have emerged as key regulators of a large number of genes. The present study aimed to explore novel biological functions of miR-330 in the human prostate cancer cell lines DU145 and PC3. We confirmed that miR-330 was downregulated and inversely correlated with specificity protein 1 (Sp1).
Overexpression of miR-330 by transfection of a chemically synthesized miR-330 mimic induced a reduction in expression levels of the Sp1 protein, accompanied by significant suppression of cellular migration and invasion capability. In addition, the Sp1-knockdown experiments presented similar phenomena. Finally, the luciferase reporter assay validated Sp1 as the direct target of miR-330. These findings indicate that miR-330 acts as an anti-metastatic miRNA in prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary  
AUTORES / AUTHORS: - Goldfarb DA

[471] TÍTULO / TITLE: - Brassinin Induces Apoptosis in PC-3 Human Prostate Cancer Cells through the Suppression of PI3K/Akt/mTOR/S6K1 Signaling Cascades.  
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary  
AUTORES / AUTHORS: - Kim SM; Park JH; Kim KD; Nam D; Shim BS; Kim SH; Ahn KS; Choi SH; Ahn KS  
INSTITUCIÓN / INSTITUTION: - College of Korean Medicine, Kyung Hee University, 1 Hoegi-Dong Dongdaemun-Gu, Seoul, 130-701, Republic of Korea.  
RESUMEN / SUMMARY: - The oncogenic PI3K/Akt/mammalian target of rapamycin (mTOR) signaling axis and its downstream effector, the ribosomal protein S6 kinase 1 (S6K1) play a key role in mediating cell survival in various tumor cells. Here, we investigated the effects of brassinin (BSN), a phytoalexin first identified as a constituent of cabbage, on the PI3K/Akt/mTOR/S6K1 activation, cellular proliferation, and apoptosis in PC-3 human prostate cancer. BSN exerted a significant dose-dependent cytotoxicity and reduced constitutive phosphorylation of Akt against androgen-independent PC-3 cells as compared to androgen-dependent LNCaP cells. Moreover, knockdown of androgen receptor (AR) by small interfering RNA enhanced the potential effect of BSN on induction of apoptosis in LNCaP cells. BSN clearly suppressed the constitutive activation of PI3K/Akt/mTOR/S6K1 signaling cascade, which correlated with the induction of apoptosis as characterized by accumulation of cells in subG1 phase, positive Annexin V binding, TUNEL staining, loss of mitochondrial membrane potential, down-regulation of antiapoptotic and proliferative proteins, activation of caspase-3, and cleavage of PARP. Additionally, BSN could block broad-spectrum inhibition of PI3K/Akt/mTOR/S6K1 axes, and aberrant Akt activation by pcDNA3-myrr-HA-Akt1 plasmid could not prevent the observed suppressive effect of BSN on constitutive mTOR activation. Finally, overexpression of Bcl-2 also attenuated BSN-mediated apoptosis in PC-3 cells. Taken together, our findings suggest that BSN can interfere with multiple signaling cascades involved in tumorigenesis and might be provided as a
potential therapeutic candidate for both the prevention and treatment of prostate cancer. Copyright © 2013 John Wiley & Sons, Ltd.

[472]

**TITULO / TITLE:** Elevated Inflammatory Markers Combined with Positive Pneumococcal Urinary Antigen are a Good Predictor of Pneumococcal Community Acquired Pneumonia in Children.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** Pediatr Infect Dis J. 2013 May 20.

**AUTORES / AUTHORS:** Galetto-Lacour A; Alcoba G; Posfay-Barbe KM; Cevey-Macherel M; Gehri M; Ochs MM; Brookes RH; Siegrist CA; Gervaix A

**INSTITUCIÓN / INSTITUTION:** 1 Division of Pediatric Emergency Medicine, 2 Department of Child and Adolescent Medicine, Geneva University Hospitals and University of Geneva, 3 Child and Adolescent Department, Lausanne, University Hospital, Switzerland; 4 sanofi pasteur, Marcy l’Etoile, France; 5 sanofi pasteur, Toronto, Canada.

**RESUMEN / SUMMARY:** BACKGROUND:: Our objective was to evaluate procalcitonin (PCT) and C-reactive protein (CRP) as predictors of a pneumococcal etiology in community-acquired pneumonia (CAP) in hospitalized children. METHODS:: Children requiring hospitalization for CAP were prospectively enrolled. The following indices were determined: antibodies against pneumococcal surface proteins (anti-Ply, PhtD, PhtE, LytB and PcpA), viral serology, naso-pharyngeal cultures and PCR for 13 respiratory viruses, blood pneumococcal PCR, pneumococcal urinary antigen (PUA), PCT and CRP. Presumed pneumococcal CAP (P-CAP) was defined as a positive blood culture or PCR for S. pneumoniae, or as a pneumococcal surface protein seroresponse (>= 2-fold increase). RESULTS:: 75 patients were included from which 37 (49%) met the criteria of P-CAP. Elevated PCT and CRP values were strongly associated with P-CAP with odds-ratios of 23 (95%CI:5-117) for PCT and 19 (95%CI:5-75) for CRP in multivariate analysis. The sensitivity was 94.4% for PCT (cut-off: 1.5 ng/mL) and 91.9% for CRP (cut-off: 100 mg/L). A value <= 0.5 ng/mL of PCT ruled out P-CAP in more than 90% of cases (negative likelihood ratio: 0.08). Conversely, a PCT value >= 1.5 ng/mL associated with a positive PUA had a diagnostic probability for P-CAP of almost 80% (positive likelihood ratio: 4.59). CONCLUSIONS:: PCT and CRP are reliable predictors of P-CAP. Low-cut off values of PCT allow identification of children at low risk of P-CAP. The association of elevated PCT or CRP with a positive PUA is a strong predictor of P-CAP.
[473]
**TÍTULO / TITLE:** - WKYMVm-induced cross-talk between FPR2 and HGF receptor in human prostate epithelial cell line PNT1A.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)


**AUTORES / AUTHORS:** - Cattaneo F; Parisi M; Ammendola R

**INSTITUCIÓN / INSTITUTION:** - Department of Biochemistry and Medical Biotechnology, University of Naples Federico II, Via S. Pansini 5, 80131 Naples, Italy.

**RESUMEN / SUMMARY:** - Cross-communication between GPCRs and TKRs represents a mechanism to amplify the information exchange throughout the cell. We show that WKYMVm, an FPR2 agonist, induces the phosphorylation of Y1313/Y1349/Y1356 residues of c-Met and triggers some of the molecular responses elicited by c-Met/HGF binding, such as STAT3, PLC-gamma1/PKCalpha and PI3K/Akt pathways. The critical role of NADPH oxidase-dependent superoxide generation in this cross-talk mechanism is supported by the finding that blockade of NADPH oxidase function prevents c-Met trans-phosphorylation and the downstream signalling cascade. These results highlight the function of FPR2 to activate an interconnected signalling network and suggest novel possibilities for therapeutic interventions.

[474]
**TÍTULO / TITLE:** - H-rev107 regulates prostaglandin D2 synthase-mediated suppression of cellular invasion in testicular cancer cells.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)


**AUTORES / AUTHORS:** - Shyu RY; Wu CC; Wang CH; Tsai TC; Wang LK; Chen ML; Jiang SY; Tsai FM

**INSTITUCIÓN / INSTITUTION:** - Department of Research, Buddhist Tzu Chi General Hospital, Taipei Branch, New Taipei City, Taiwan. 

**RESUMEN / SUMMARY:** - BACKGROUND: H-rev107 is a member of the HREV107 type II tumor suppressor gene family which includes H-REV107, RIG1, and HRASLS. H-REV107 has been shown to express at high levels in differentiated tissues of post-meiotic testicular germ cells. Prostaglandin D2 (PGD2) is conjectured to induce SRY-related high-mobility group box 9 (SOX9) expression and subsequent Sertoli cell differentiation. To date, the function of
H-rev107 in differentiated testicular cells has not been well defined. RESULTS: In the study, we found that H-rev107 was co-localized with prostaglandin D2 synthase (PTGDS) and enhanced the activity of PTGDS, resulting in increase of PGD2 production in testis cells. Furthermore, when H-rev107 was expressed in human NT2/D1 testicular cancer cells, cell migration and invasion were inhibited. Also, silencing of PTGDS would reduce H-rev107-mediated increase in PGD2, cAMP, and SOX9. Silencing of PTGDS or SOX9 also alleviated H-rev107-mediated suppression of cell migration and invasion. CONCLUSIONS: These results revealed that H-rev107, through PTGDS, suppressed cell migration and invasion. Our data suggest that the PGD2-cAMP-SOX9 signal pathway might play an important role in H-rev107-mediated cancer cell invasion in testes.

[475]

**TITULO / TITLE:** Ataxia-telangiectasia and wilms tumor: reduced treatment but early relapse.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


● Enlace al texto completo (gratuito o de pago) 1097/MPH.0b013e31828fccdf

**AUTORES / AUTHORS:** Perez-Villena A; Cormenzana M; Prada Id; Perez-Martinez A; Aleo E

**INSTITUCIÓN / INSTITUTION:** Divisions of *Paediatric Haematology and Oncology daggerPathology, Hospital Infantil Universitario Nino Jesus, Madrid, España.

**RESUMEN / SUMMARY:** Ataxia-telangiectasia (A-T) is an autosomal recessive disease characterized by progressive cerebellar ataxia, oculocutaneous telangiectasia, immunodeficiency, a high incidence of lymphoreticular tumors, and an increased sensitivity to chemoradiotherapy-induced DNA damage. The appropriate cancer therapy remains unknown because of high toxicity rates with full-dose conventional protocols. We present a patient with A-T and nephroblastoma, who received an adapted treatment regimen. To our knowledge this is the second report on nephroblastoma in a patient with A-T but the first with confirmed premortem studies. Although the patient tolerated the chemotherapy regimen well, the patient relapsed and died a year after initial diagnosis.

[476]
TÍTULO / TITLE: - High-grade Transitional Cell Carcinoma of the Bladder in a 5-Year-Old Boy Successfully Treated With Partial Cystectomy and Intravesical Bacillus Calmette-Guerin.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Khandelwal P; Brewer AJ; Minevich E; Miles L; Geller JI

INSTITUCIÓN / INSTITUTION: - Divisions of *Oncology, Cancer, and Blood Diseases Institute daggerPathology double daggerPediatric Urology, Cincinnati Childrens Hospital Medical Center, Cincinnati, OH.

RESUMEN / SUMMARY: - Pediatric transitional cell carcinomas of the bladder are typically characterized by low-grade histology, adolescent and young adult age, and cure with surgical resection. Here, we report a high-grade transitional cell carcinoma of the bladder in a 5-year-old boy treated with a partial cystectomy and adjuvant intravesical Bacillus Calmette-Guerin.

[477]

TÍTULO / TITLE: - Safety and feasibility of Laparoscopic Radical Cystectomy for the treatment of bladder cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Aboumarzouk OM; Hughes O; Narahari K; Drewa T; Chlosta PL; Kynaston H

INSTITUCIÓN / INSTITUTION: - Wales Deanery, Urology, Cardiff, Wales, United Kingdom ; aboumarzouk@gmail.com.

RESUMEN / SUMMARY: - Introduction: Radical cystectomy is the mainstay of the management of muscle invasive bladder cancer. Numerous centres have adopted a minimally invasive approach to replace the standard open procedure. Objectives: To review published literature comparing laparoscopic and open radical cystectomy. Material and Methods: A systematic review of the literature according to Cochrane guidelines was conducted (1993 to 2012) for studies comparing laparoscopic and open radical cystectomy. All studies comparing the two procedures were included. The outcome measures were the patient demographics, operating time, blood loss, transfusion rates, time to oral intake, length of hospital stay, and complications. A meta-analysis was conducted. For continuous data, a Mantel-Haenszel Chi-square test was used and for dichotomous data an Inverse Variance was used and each expressed as risk ratio with 95% CI. P <0.05 was considered significant. Results: Four hundred twenty-seven patients were included, 211 patients in the laparoscopic group and 216 patients in the open group (8 studies). There was no significant
difference between the two groups in any of the demographic parameters except for age (Age: P<0.0001; Sex: P=0.1; BMI: P=0.05). The laparoscopic group had significantly longer operative times (P<0.0001), however, less blood loss (P<0.00001), transfusion rates (P<0.0001), less time to oral intake (<0.0001), less analgesic requirement (P=0.0009), and shorter length of hospital stay (<0.0001). The ORC group developed significantly more minor complications than the LRC group (P=0.02). There was no difference between the two groups regarding lymph node dissection yields, major complications, positive margins, pathological results, local recurrence, or distant metastases (all P>0.05). However, there were significantly more positive nodes in the ORC group.

**Conclusion:** In experienced hands, LRC is a feasible and safe alternative to ORC with less blood loss, transfusion and analgesic requirement, shorter lengths of hospital stay, and less complications, however, does have longer operative times.
[479]
TÍTULO / TITLE: - Re: increased incidence of penile cancer and high-grade penile intraepithelial neoplasia in Denmark 1978-2008: a nationwide population-based study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wood DP

[480]
TÍTULO / TITLE: - Estrogen receptor-beta expression and pharmacological targeting in bladder cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kauffman EC; Robinson BD; Downes M; Marcinkiewicz K; Vourganti S; Scherr DS; Gudas LJ; Mongan NP
INSTITUCIÓN / INSTITUTION: - Department of Urology, Weill Cornell Medical College, New York, NY 10065, USA.
RESUMEN / SUMMARY: - A role for estrogen signaling in urothelial carcinoma of the bladder (UCB) is suggested to be associated with more advanced disease with worse outcomes in women. Estrogen receptor beta (ERbeta) is the predominant receptor in bladder tissues. We aimed to ascertain whether ERbeta correlates with clinicopathological predictors of aggressive bladder cancer and worse survival outcomes. ERbeta was measured by immunohistochemistry in malignant and adjacent benign bladder tissues in patients (N=72) with UCB who underwent radical cystectomy. ERbeta expression was tested for statistical association with clinicopathological variables and patient survival. ERbeta expression was determined in bladder cancer cell lines, and the effects of the selective estrogen modulator tamoxifen and the ERbeta agonist diarylpropionitrile on cell growth were determined. The ERbeta level was significantly higher in malignant vs. benign urothelium (P<0.001) and was strongly associated with aggressive tumor histology characterized by lymphovascular (P=0.008) and perineural (P=0.006) invasion, and clinical histories of pelvic irradiation (P=0.005), hydronephrosis (P=0.022) and no intravesical chemotherapy (P=0.038). All patients with a high (>70%) percentage of ERbeta positivity in tissue with >3-month follow-up developed recurrent disease (P=0.009). Higher ERbeta level was predictive of worse recurrence-free and overall survival following cystectomy, after adjustment for
tumor stage, and remained significantly associated with recurrence-free survival in the multivariable analysis including tumor stage, nodal stage and lymphovascular invasion. Activation of ERβ in bladder cancer cell lines led to significant increases in proliferation, while pharmacological inhibition with tamoxifen blocked cell growth. Our study supports a role for ERβ in aggressive UCB. Pharmacological targeting of ERβ warrants further investigation as a therapeutic strategy in UCB.

[481]

TÍTULO / TITLE: - The prostate cancer-up-regulated Myc-associated zinc-finger protein (MAZ) modulates proliferation and metastasis through reciprocal regulation of androgen receptor.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Jiao L; Li Y; Shen D; Xu C; Wang L; Huang G; Chen L; Yang Y; Yang C; Yu Y; Sun Y

INSTITUCIÓN / INSTITUTION: - Department of Urology, Changhai Hospital, Second Military Medical University, 168 Changhai Road, Shanghai 200433, P. R. China. 36705487@qq.com

RESUMEN / SUMMARY: - Prostate cancer (PCa) is one of the most commonly diagnosed malignancies in men and the second leading cause of male cancer mortality. MAZ (Myc-associated zinc-finger protein) is a transcription factor that regulates the transcription of oncogenes, and the deregulated MAZ expression is closely related to the development and progression of a variety of cancers. In the present study, the role of MAZ in PCa tumorigenesis and its interaction with androgen receptor (AR), which is essential to PCa development in humans, were investigated. MAZ expression was found to be higher in clinical PCa specimens than in benign prostatic hyperplasia (BPH) and adjacent normal tissues, and MAZ expression was positively correlated with AR expression, which was also observed in PCa cell lines. After knockdown of MAZ by siRNA, cell proliferation was notably inhibited, colony formation declined, the cell cycle was arrested at G0/G1 phase, and the number of cells in S phase decreased (p < 0.05). MAZ knockdown resulted in a significant decline in the migration and invasion capacity of the LNCaP-AD cell line. siRNA knockdown of AR significantly decreased MAZ expression, and knockdown of MAZ significantly increased the expression of AR and DHT-induced androgen response element (ARE). These results suggest that MAZ and AR are interrelated and that MAZ plays an important role in PCa pathogenesis, which could be a potential therapeutic target.
TÍTULO / TITLE: Conditional survival after nephrectomy for renal cell carcinoma (RCC): changes in future survival probability over time.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Bianchi M; Becker A; Hansen J; Trinh QD; Tian Z; Abdollah F; Briganti A; Shariat SF; Perrotte P; Montorsi F; Karakiewicz PI; Sun M

INSTITUCIÓN / INSTITUTION: Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, Canada; Department of Urology, Vita-Salute San Raffaele University, Milan, Italy.

RESUMEN / SUMMARY: OBJECTIVE: To examine the impact of length of survival on future survival probability, otherwise known as the effect of conditional survival (CS), after nephrectomy (NT) in patients diagnosed with renal cell carcinoma (RCC). PATIENTS AND METHODS: Overall, 42 090 patients with RCC who underwent NT were abstracted from the Surveillance, Epidemiology, and End Results database (1988-2008). Based on cumulative survival estimates, CS rates were derived according to patient and disease characteristics. Separate multivariable Cox regression analyses were performed for the prediction of cancer-specific mortality (CSM), according to 1-, 2-, 3-, 4- and 5-year survival postoperatively. RESULTS: Immediately after surgery, the 5-year cancer-specific survival rate was 83.5%. Amongst patients who survived >/=1, >/=2, >/=3, >/=4, and >/=5 years after NT, the probability rates for surviving an additional 5 years were 87.0, 89.6, 90.9, 92.0 and 92.3%, respectively. Provided that patients survived 1 and 2 years after NT, the probability of being CSM-free for another 5 years increased by +4.1 and 4.3% for stage III and +12.9 and 10.3% for stage IV disease, respectively. Similar observations were recorded for patient age, grade, nodal stage and tumour size, and were confirmed upon multivariable analyses. CONCLUSION: Survival probabilities vary according to length of survival after NT. Specifically, even amongst patients with more advanced disease at surgery, a more favourable prognosis can be achieved after surviving for 1-2 years.

TÍTULO / TITLE: The effect of anti-human leukocyte antigen, anti-major histocompatibility complex class 1 chain-related antigen a, and anti-glutathione transferase-t1 antibodies on the long-term survival of renal allograft.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
BACKGROUND: One of the most important mechanisms of allograft rejection is the production of donor-specific antibodies (DSA). Anti-major histocompatibility complex class-I chain-related antigen A (MICA) and anti-glutathione S transferase-T1 (GSTT1) antibodies cause graft dysfunction and reduce graft survival. The aim of this study was to examine the effects of anti-human leukocyte antigen class I-II, anti-MICA, and anti-GSTT1 antibodies in development of antibody-mediated rejection. METHODS: Among the 32 renal transplant patients included in this study 65% experienced antibody-mediated rejection (AMR; chronic active AMR [CAMR], n = 17; acute AMR [AAMR], n = 4) and 35%, ACR. The anti-HLA class I-II and anti-MICA antibodies were determined by using LUMINEX, anti-GSTT1 antibodies by enzyme-linked immunosorbent assay. GSTT1 genotyping of patients and donors was performed by polymerase chain reaction. RESULTS: Antibody was detected in 19 of 21 patients undergoing antibody-mediated rejection (90%). We detected anti-GSTT1 in 4, anti-MICA in 8, anti-HLA class I in 5, and anti-HLA class II in 9 patients with CAMR (P = .007). If the patients were divided into 2 groups according to being C4d(+) and C4d(-) both anti-HLA class I and class II antibodies were found significantly more frequently among the C4d(+) group (P = .019, P = .024). No difference was determined between AMR and ACR groups in terms of anti-GSTT1 and anti-MICA antibodies. CONCLUSIONS: In this study, we observed the role of anti-HLA class II antibodies in the development of CAMR and in long-term allograft survival. It is observed that anti-MICA and anti-GSTT1 antibodies showed no effect on rejection mechanisms.

[484]
AUTORES / AUTHORS: Hsu WH; Yu YR; Hsu SH; Yu WC; Chu YH; Chen YJ; Chen CM; You LR
INSTITUCIÓN / INSTITUTION: Institute of Biochemistry and Molecular Biology, National Yang-Ming University, Taipei 112, Taiwan.
RESUMEN / SUMMARY: Coronin 1B es crucial para la motilidad celular y varios procesos dependientes de actina. Para entender mejor su rol, se exploró la expresión y regulación transcripcional del gen Coro1b durante el desarrollo embrionario de la rata. Coronin 1B es expresado universalmente en el embrión completo, pero muestra un patrón de expresión distintivo en el corazón, en particular en el endocardio y epicardio donde se producen los procesos EMT. Se identificaron los posiciones entre -1038 y -681 como importantes para la actividad promotora basal del gen Coro1b. Se identificaron secuencias posibles de unión del Wt1 en el promotor del gen Coro1b. El enlace de Wt1 a secuencias ricas en GC es necesario para la regulación de la expresión del gen Coro1b. En línea con la disminución de movilidad encontrada en células Knockdown de Coronin 1B, se observó una modesta disminución en la expresión de Coronin 1B en el epicardio restante de embiones mutantes Wt1(EGFPCre/EGFPCre) durante el desarrollo del corazón. Estos hallazgos sugieren que el Wt1 puede desempeñar un papel en el control transcripcional de la expresión del gen Coro1b.

TÍTULO / TITLE: GATA3 expression in paragangliomas: a pitfall potentially leading to misdiagnosis of urothelial carcinoma.
RESUMEN / SUMMARY: GATA3 es un factor de transcripción con unión al zinc, que se expresa en varios tejidos normales y neoplásicos. Entre los tumores, se etiqueta como carcinoma de vejiga, carcinoma de los conductos colectores, cáncer de mama, linfoma y, de forma menos habitual, carcinoma endometrial. Pocos estudios han investigado su positividad en neoplasmas que pueden simular neoplasmas de vejiga. En este estudio, evaluamos la expresión de GATA3 en parangliomas vesicales que pueden simular neoplasmas de vejiga. Encontramos una alta expresión de GATA3 en parangliomas, lo que puede causar confusión con el carcinoma de vejiga.


TÍTULO / TITLE: GATA3 expression in paragangliomas: a pitfall potentially leading to misdiagnosis of urothelial carcinoma.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: So JS; Epstein JI
INSTITUCIÓN / INSTITUTION: Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, MD, USA.
RESUMEN / SUMMARY: GATA3 es un factor de transcripción con unión al zinc, que se expresa en varios tejidos normales y neoplásicos. Entre los tumores, se etiqueta como carcinoma de vejiga, carcinoma de los conductos colectores, cáncer de mama, linfoma y, de forma menos habitual, carcinoma endometrial. Pocos estudios han investigado su positividad en neoplasmas que pueden simular neoplasmas de vejiga. En este estudio, evaluamos la expresión de GATA3 en parangliomas vesicales que pueden simular neoplasmas de vejiga. Encontramos 12 casos de parangliomas vesicales que se asemejan al carcinoma de vejiga y 20 casos de
paragangliomas from non-urologic sites using the Hopkins Pathology Data Base system. GATA3 was positive in 10 of the 12 (83%) urinary bladder paragangliomas studied on routine slide sections. Most (6/12) of the staining was diffusely strong (3+) staining, whereas the rest (4/12) that were positive showed mixed intensities (strong 3+ to moderate 2+). The 20 paragangliomas from other sites were constructed into tissue microarrays, wherein three cores from each tumor were taken. Fifteen out of 20 (75%) paragangliomas outside of the bladder were positive for GATA3 staining. Moderate (2+) or strong (3+) staining was seen in 13/20 (65%) of extravesical paragangliomas, ranging from 5 to 100% of the cell labeling (mean 59%, median 60%). In the remaining 7/20 (35%) cases, only weak (2/7) or negative (5/7) immunoreactivity for GATA3 was seen. An additional 15 cases of metastatic paraganglioma from various primary sites were retrieved with 12 of 15 (80%) metastatic paragangliomas staining positively for GATA3. Overall, for paragangliomas, regardless of site, 78.7% were positive for GATA3. Recognition of this finding will aid pathologists in preventing a misdiagnosis of a urothelial tumor based on GATA3 expression, which is critical given the differences in treatment, follow-up and prognosis between bladder paragangliomas and urothelial carcinoma. Modern Pathology advance online publication, 19 April 2013; doi:10.1038/modpathol.2013.76.

RESUMEN / SUMMARY: - In this review, the role of surgery in patients with adverse tumor characteristics and a high risk of tumor progression are discussed. In the current PSA era the proportion of patients presenting with high risk prostate cancer (PCa) is estimated to be between 15% and 25% with a 10-year cancer specific survival in the range of 80-90% for those receiving active local treatment. The treatment of high risk prostate cancer is a contemporary challenge. Surgery in this group is gaining popularity since 10-year cancer specific survival data of over 90% has been described. Radical prostatectomy should be combined with extended lymphadenectomy. Adjuvant or salvage therapies may be needed in more than half of patients, guided by pathologic findings and postoperative PSA. Unfortunately there are no randomized controlled trials comparing radical prostatectomy to radiotherapy and no single treatment can be universally recommended. This group of high risk prostate cancer patients should be considered a multi-disciplinary challenge; however, for the properly selected patient, radical prostatectomy either as initial or as the only therapy can be considered an excellent treatment.

[488]

TÍTULO / TITLE: - Algorithms for the determination of unacceptable HLA antigen mismatches in kidney transplant recipients.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Susal C; Roelen DL; Fischer G; Campos EF; Gerbase-Delima M; Honger G; Schaub S; Lachmann N; Martorell J; Claas F

INSTITUCIÓN / INSTITUTION: - Department of Transplantation Immunology, Institute of Immunology, University of Heidelberg, Heidelberg, Germany.

RESUMEN / SUMMARY: - One of the major tasks of human leukocyte antigen (HLA) laboratories is the pretransplant determination of unacceptable HLA antigen mismatches (UAM) in organ transplant recipients. HLA antigen specificities are determined against which the patient has circulating alloantibodies that are expected to harm the transplanted organ. Using the information on UAM, negative crossmatch (XM) prediction or ‘virtual XM’ is possible when a potential donor’s complete HLA typing is available. Before the introduction of solid-phase antibody detection assays, UAM were determined using the complement-dependent cytotoxicity methodology. After the introduction of the single antigen bead technique, however, various UAM determination algorithms have emerged. In this report, six different laboratories worldwide present how they determine UAM in their collective of kidney
transplant recipients in the pretransplant phase and proceed thereafter to transplantation.

[489]
**TÍTULO / TITLE:** - The role of surgery for metastatic renal cell carcinoma in the era of targeted therapies.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Bigot P; Lebdai S; Ravaud A; Azzouzi AR; Ferriere JM; Patard JJ; Bernhard JC

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Angers University Hospital, Angers, France, pibigot@chu-angers.fr.

**RESUMEN / SUMMARY:** - PURPOSE: With the emergence of targeted therapies, the indications of cytoreductive nephrectomy have to be redefined. This review article presents the evidence data guiding our current indications of surgery in the management of metastatic renal cell carcinoma (mRCC) in the era of targeted therapies. METHODS: A nonsystematic review of the electronic databases PubMed and MEDLINE from 1980 to 2012 was performed and limited to English language. RESULTS: Two studies based on immunotherapy (EORTC 30947 and SWOG 8949) were at the origins of the recommendations on initial nephrectomy for patients with mRCC. Since the introduction of angiogenesis inhibitors, there is still no high-level evidence from prospective studies assessing the indication of surgery for mRCC. However, surgery still has its importance in the management of primary tumors and metastasis with the objective of an optimal balance between morbidity, quality of life, and survival. The treatment sequence between surgery and targeted therapies is still to be established and two randomized prospective studies were then specifically designed and are currently recruiting. CONCLUSIONS: Preliminary evidence data from retrospective series seem to be in favor of a benefit of surgery for patients with good and intermediate prognosis. However, patients’ inclusions in current prospective studies are highly recommended to clearly precise nephrectomy’s indications.

[490]
**TÍTULO / TITLE:** - TAK-441, a novel investigational smoothened antagonist, delays castration-resistant progression in prostate cancer by disrupting paracrine hedgehog signaling.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

Hedgehog (Hh) signaling is a highly conserved intercellular and intracellular communication mechanism that governs organogenesis and is dysregulated in cancers of numerous tissues, including prostate. Up-regulated expression of the Hh ligands, Sonic (Shh) and Desert (Dhh), has been reported in androgen-deprived and castration-resistant prostate cancer (CRPC). In a cohort of therapy naive, short- and long-term neoadjuvant hormone therapy-treated (NHT), and CRPC specimens, we observed elevated Dhh expression predominantly in long-term NHT specimens and elevated Shh expression predominantly in CRPC specimens. Together with previously demonstrated reciprocal signaling between Shh-producing prostate cancer (PCa) cells and urogenital mesenchymal fibroblasts, these results suggest that castration-induced Hh expression promotes CRPC progression through reciprocal paracrine signaling within the tumor microenvironment. We tested whether the orally available Smoothened (Smo) antagonist, TAK-441, could impair castration-resistant progression of LNCaP PCa xenografts by disrupting paracrine Hh signaling. Although TAK-441 or cyclopamine did not affect androgen withdrawal-induced Shh up-regulation or viability of LNCaP cells, castration-resistant progression of LNCaP xenografts was significantly delayed in animals treated with TAK-441. In TAK-441-treated xenografts, expression of murine orthologs of the Hh-activated genes, Gli1, Gli2 and Ptc1, was substantially suppressed, while expression of the corresponding human orthologs was unaffected. As androgen-deprived LNCaP cells up-regulate Shh expression, but are not sensitive to Smo antagonists, these studies indicate that TAK-441 leads to delayed castration-resistant progression of LNCaP xenografts by disrupting paracrine Hh signaling with the tumor stroma. Thus, paracrine Hh signaling may offer unique opportunities for prognostic biomarker development, drug targeting and therapeutic response monitoring of PCa progression.

[491]

Utilization of a TFE3 Break-apart FISH Assay in a Renal Tumor Consultation Service.

Enlace al Resumen / Link to its Summary

Xp11 translocation renal cell carcinomas (RCCs) are characterized by chromosome translocations involving the Xp11.2 breakpoint, resulting in gene fusions involving the TFE3 transcription factor. In archival material, the diagnosis can often be confirmed by TFE3 immunohistochemistry (IHC), but variable fixation (especially prevalent in consultation material) can lead to equivocal results. A TFE3 break-apart fluorescence in situ hybridization (FISH) assay has been developed to detect TFE3 gene rearrangements; however, the utility of this assay in a renal tumor consultation practice has not been examined. We reviewed 95 consecutive renal tumor consultation cases submitted to rule in or rule out Xp11 translocation RCC. Thirty-one cases were positive for TFE3 rearrangements by FISH. Patients ranged from 6 to 67 years of age (mean=30 y; median=28 y). Novel or distinctive morphologic features of these cases included extensive cystic change simulating multilocular cystic RCC (3 cases), sarcomatoid transformation (3 cases), oncocytic areas mimicking oncocytoma (1 case), trabecular architecture mimicking a carcinoid tumor (1 case), colonization of renal pelvic urothelium mimicking urothelial carcinoma in situ (1), and focal desmin and diffuse racemase immunoreactivity (1 case each). Twenty-six of the 31 TFE3 FISH-positive RCCs were unequivocally positive for TFE3 by IHC, but 4 were equivocal, and 1 was negative. Of the 64 cases that were negative by TFE3 FISH, 50 were negative by TFE3 IHC, and 14 were equivocal. Thirty-two of the 64 TFE3 FISH-negative cases could be classified into other accepted RCC subtypes: 23 as clear cell RCC, 5 as papillary RCC, 3 as clear cell papillary RCC, and 1 as chromophobe RCC. The other 32 cases remained unclassified, including 3 cathepsin K-positive RCC that closely resembled Xp11 translocation RCC. In conclusion, TFE3 FISH is highly useful in renal tumor consultation material, often resolving cases with equivocal TFE3 IHC results. Given the difficulty of optimizing TFE3 IHC, TFE3 FISH is for most laboratories the optimal test for establishing the diagnosis of Xp11 translocation RCC.
OBJECTIVE: To investigate the influence of diabetes mellitus (DM) on late genitourinary (GU) and gastrointestinal (GI) toxicity in patients treated with external beam radiotherapy (RT) for prostate cancer.

MATERIALS AND METHODS: A total of 626 men were treated with curative-intent RT for prostate cancer from 1988 to 2008. Using the National Comprehensive Cancer Network risk category, the patients were considered to have low-risk (30%), intermediate-risk (42%), or high-risk (28%) prostate cancer. The median radiation dose was 74 Gy; 45% received androgen deprivation therapy for a median of 4 months. Late GU and GI Radiation Therapy Oncology Group toxicity was recorded prospectively at each visit after external beam RT. The median follow-up period was 55 months.

RESULTS: Of the 626 men, 102 (16%) had DM that was controlled by diet (8%), oral medications (52%), or insulin (39%). The patients with DM were more likely to receive intensity-modulated RT and androgen deprivation therapy and to have a shorter follow-up duration (\( P \leq 0.05 \) for all). Univariate analyses demonstrated that greater radiation dose, baseline urinary dysfunction, intensity-modulated RT, and DM were associated with grade 2 or greater GU toxicity, and transurethral resection of the prostate and DM were associated with grade 3 or greater GU toxicity. In addition, androgen deprivation therapy use, age \( \geq 70 \) years, and anticoagulation were associated with grade 2 or greater GI toxicity, and age \( \geq 70 \) years and anticoagulation were associated with grade 3 or greater GI toxicity. The multivariate analyses for late toxicity demonstrated a greater risk of grade 2 or greater (relative risk 1.36, \( P = 0.10 \)) and grade 3 or greater GU toxicity (relative risk 2.74, \( P = 0.04 \)) with DM. CONCLUSION: A greater incidence of late GU toxicity was seen in patients with DM treated for prostate cancer. This relationship might be useful when considering the treatment of patients with DM, especially those receiving dose-escalated RT or with a history of transurethral resection of the prostate.
RESUMEN / SUMMARY: - PURPOSE: Published efficacy and safety data from clinical trials of three recently approved agents for the management of metastatic castration-resistant prostate cancer (CRPC) are reviewed.

SUMMARY: Sipuleucel-T is approved by the Food and Drug Administration (FDA) for the treatment of asymptomatic or minimally symptomatic patients with CRPC. In a placebo-controlled Phase III clinical trial, the use of sipuleucel-T was associated with an average improvement in median overall survival of 4.1 months. Abiraterone acetate and cabazitaxel are approved by FDA as second-line treatments for patients with CRPC who experience disease progression during first-line docetaxel therapy. In Phase III trials, abiraterone acetate was associated with improved overall survival relative to placebo use (14.8 months versus 10.9 months), and cabazitaxel was found to confer an overall survival advantage over mitoxantrone therapy (median survival, 15.1 months versus 12.7 months), corresponding to a 30% reduction in the relative risk of death (hazard ratio, 0.7; 95% confidence interval, 0.59-0.83; p < 0.0001). The three agents range in cost from $40,000 to $93,000 for a full course of therapy. Sipuleucel therapy entails leukapheresis procedures for the collection of autologous cells used in dose preparation, requiring careful planning and coordination of care. CONCLUSION: Sipuleucel-T, abiraterone acetate, and cabazitaxel offer new options for the treatment of patients with CRPC, including those with disease resistant to standard first-line therapies. The agents’ varying administration requirements, as well as patient-specific factors and cost issues, are key considerations in the drug selection process.

[494]

TÍTULO / TITLE: - Human Prostate Stem Cell Antigen and HSP70 Fusion Protein Vaccine Inhibits Prostate Stem Cell Antigen-expressing Tumor Growth in Mice.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Dong L; Zhang X; Ren J; Wu S; Yu T; Hou L; Fu L; Yi S; Yu C

INSTITUCIÓN / INSTITUTION: - 1 Clinical Laboratory Center, PLA Air Force General Hospital, Beijing, China.

RESUMEN / SUMMARY: - Abstract Prostate stem cell antigen (PSCA) has been considered a potentially worthwhile target for prostate cancer therapy with its overexpression in both androgen-dependent and androgen-independent prostate cancers. However, PSCA is an autoantigen that can evoke immunological tolerance and hardly incite effective immunologic response. In this study, we sought to construct the fusion protein vaccines based on PSCA
and heat shock protein 70 (HSP70) and to evaluate their immune responses and therapeutic efficacy. A series of recombinant proteins were prepared, and then, the male C57BL/6 mice were immunized subcutaneously by inoculation with RM-PSCA/Luc cells. The PSCA-specific cellular immune responses were monitored with ELISPOT and intracellular cytokines staining assay, and ELISA assay was used to detect humoral immune responses. The tumor growth was observed by in vivo bioluminescence imaging. The results showed that the mice vaccinated with PSCA-HSP could induce the PSCA-specific cellular and humoral immune responses. Tumor progression could be quantitatively monitored by in vivo bioluminescence imaging. Animal experiments showed that PSCA-HSP could inhibit the growth of PSCA-expressing tumors and prolong the survival time of vaccinated mice. This study supported and confirmed the potential of HSP70 as a chaperone for protein vaccines, and PSCA-HSP could be of potential value for prostate cancer treatment.

[495]

TÍTULO / TITLE: miR-192, miR-194 and miR-215: A Convergent miRNA Network Suppressing Tumor Progression in Renal Cell Carcinoma.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 1093/carcin/bgt184

AUTORES / AUTHORS: Khella HW; Bakhet M; Allo G; Jewett MA; Girgis AH; Latif A; Girgis H; Von Both I; Bjarnason GA; Yousef GM

INSTITUCIÓN / INSTITUTION: Department of Laboratory Medicine and the Keenan Research Centre in the Li Ka Shing Knowledge Institute of St. Michael’s Hospital, Toronto, ON, M5B 1W8, Canada.

RESUMEN / SUMMARY: miRNAs play a crucial role in tumor progression and metastasis. We and others recently identified a number of miRNAs that are dysregulated in metastatic, compared to primary renal cell carcinoma (RCC). Here, we investigated three miRNAs that are significantly downregulated in metastatic tumors; miR-192, miR-194 and miR-215. Gain-of-function analyses showed that restoration of their expression decreases cell migration and invasion in RCC cell line models, while knockdown of these miRNAs resulted in enhancing cellular migration and invasion abilities. We identified three targets of these miRNAs with potential role in tumor aggressiveness; MDM2, TYMS, and SIP1/ZEB2. We observed a convergent (the same molecule can be targeted by all three miRNAs) and a divergent (the same miRNA can control multiple targets) effects for these miRNAs. We experimentally validated these miRNA-target interactions using three independent approaches. First, we observed that miRNA overexpression significantly reduces the mRNA and protein levels of their targets. In the second, we observed significant reduction of the luciferase signal of a vector containing the 3’UTR of the target upon miRNA
Finally, we show the presence of inverse correlation between miRNA changes and the expression levels of their targets in patient specimens. We also examined the prognostic significance of miR-215 in RCC. Lower expression of miR-215 is associated with significantly reduced disease-free survival time. These findings were validated on an independent dataset from The Cancer Genome Atlas. These results can pave the way to the clinical use of miRNAs as prognostic markers and therapeutic targets.
Mohs surgery in metastatic cancer: renal cell carcinoma solitary cutaneous metastasis and visceral tumor metastases to skin treated with microscopically controlled surgical excision.

BACKGROUND: Mohs micrographic surgery is the reference standard treatment for primary cutaneous malignancies.

OBJECTIVES: The purpose of this case study is to demonstrate that Mohs surgery may be considered as a possible treatment for a solitary metastatic tumor under the appropriate circumstances.

METHODS: We report a patient in whom a solitary cutaneous metastasis of renal cell carcinoma (RCC) was successfully treated with microscopically controlled surgical excision, and cite instances of the successful management of cutaneous metastases using the Mohs surgical technique in oncology patients reported in the literature. Patient reports and previous reviews of the subject were critically assessed. Salient features are presented.

RESULTS: Metastases to the skin are rare in RCC. Albeit rarely, surgical excision, particularly Mohs micrographic surgery, has been used for the removal of isolated RCC cutaneous metastases. In the present patient with metastatic RCC, a solitary cutaneous metastasis on the occipital scalp was successfully treated with Mohs micrographic surgery. There was no recurrence of the lesion after two years of follow-up; however, the patient eventually succumbed to progressive disease.

CONCLUSIONS: We suggest that, in the appropriate setting, surgical excision of isolated cutaneous metastases using microscopically controlled margins at the time of surgery should be added to the indications for Mohs surgery.

Interactional expression of netrin-1 and its dependence receptor UNC5B in prostate carcinoma.

BACKGROUND: Mohs micrographic surgery is the reference standard treatment for primary cutaneous malignancies.

OBJECTIVES: The purpose of this case study is to demonstrate that Mohs surgery may be considered as a possible treatment for a solitary metastatic tumor under the appropriate circumstances.

METHODS: We report a patient in whom a solitary cutaneous metastasis of renal cell carcinoma (RCC) was successfully treated with microscopically controlled surgical excision, and cite instances of the successful management of cutaneous metastases using the Mohs surgical technique in oncology patients reported in the literature. Patient reports and previous reviews of the subject were critically assessed. Salient features are presented.

RESULTS: Metastases to the skin are rare in RCC. Albeit rarely, surgical excision, particularly Mohs micrographic surgery, has been used for the removal of isolated RCC cutaneous metastases. In the present patient with metastatic RCC, a solitary cutaneous metastasis on the occipital scalp was successfully treated with Mohs micrographic surgery. There was no recurrence of the lesion after two years of follow-up; however, the patient eventually succumbed to progressive disease.

CONCLUSIONS: We suggest that, in the appropriate setting, surgical excision of isolated cutaneous metastases using microscopically controlled margins at the time of surgery should be added to the indications for Mohs surgery.
RESUMEN / SUMMARY: - Acting via its receptor UNC5B, netrin-1, one of the major neuronal guidance cues, plays an important role in angiogenesis, neurogenesis, tissue morphogenesis, embryonic development, cancer, inflammation, and various pathologies. However, its role has not been reported in prostate carcinoma. To investigate the association of netrin-1 and UNC5B expression with prostate carcinoma, several human prostate carcinoma cell lines were cultured and the expression levels of netrin-1 and UNC5B were determined by real-time PCR and Western blot. Calphostin C, (the inhibitor of PKC alpha) and phorbol-12-myristate 13-acetate-PMA (the agonist of PKC alpha) were used to treat the prostate carcinoma cells, and the cell proliferation and invasion abilities were measured by CCK-8 and wound-healing assays. Proliferation of DU145 cells was affected by the recruitment of PMA and calphostin C in a dose-dependent manner. By immunofluorescence, we identified the localization of netrin-1 and UNC5B in prostate carcinoma cell lines (DU145, 22RV1, PC3, PC3M, and RWEP) and found that netrin-1 was highly expressed in the nucleolus but there was no expression of UNC5B. The co-localization expression of PKC alpha and UNC5B was confirmed by the confocal immunofluorescence. Higher netrin-1 and lower UNC5B expression in all prostate carcinoma cell lines indicated that netrin-1 and UNC5B could be used to predict metastasis.

[499]
TÍTULO / TITLE: - Structural and Functional Interactions of the Prostate Cancer Suppressor NKX3.1 with Topoisomerase I.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1042/BJ20130012
AUTORES / AUTHORS: - Song LN; Bowen C; Gelmann EP
RESUMEN / SUMMARY: - NKX3.1 is a prostate tumor suppressor protein that binds to topoisomerase I and enhances its DNA cleavage activity. We show that the NKX3.1 homeodomain binds to a region of topoisomerase I spanning the junction between core and linker domains. NKX3.1 activated N-terminal truncated topoisomerase I (Topo70) in vitro. In contrast, NKX3.1 interacts with the enzyme reconstituted from peptide fragments of core domain and linker-active site domains, but inhibits the DNA unwinding activity of the reconstituted enzyme in vitro. The effect of NKX3.1 on both Topo70 and the reconstituted enzyme was seen in the presence and absence of camptothecin. Neither NKX3.1 nor camptothecin had an effect on the interaction of the other with topoisomerase I. Therefore the interactions of NKX3.1 and camptothecin with the linker domain of topoisomerase I are mutually exclusive. However, in cells the effect of NKX3.1 on topoisomerase binding to DNA sensitized cells to cellular toxicity and induction of apoptosis by low dose CPT. Lastly,
topoisomerase I is important for the effect of NKX3.1 on cell survival after DNA damage as topoisomerase knockdown blocked the effect of NKX3.1 on clonogenicity after DNA damage. Therefore, NKX3.1 and topoisomerase I interact in vitro and in cells to affect CPT sensitivity and DNA repair functions of NKX3.1.

[500]

TÍTULO / TITLE: - Comparative Effectiveness Review: Prostate Cancer Antigen 3 Testing for the Diagnosis and Management of Prostate Cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Bradley LA; Palomaki GE; Gutman S; Samson D; Aronson N

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Laboratory Medicine, Women & Infants Hospital/Alpert Medical School of Brown University, Providence, Rhode Island. Electronic address: lbradley@ipmms.org.

RESUMEN / SUMMARY: - PURPOSE: We compared the effectiveness of PCA3 (prostate cancer antigen 3) and select comparators for improving initial or repeat biopsy decision making in men at risk for prostate cancer, or treatment choices in men with prostate cancer. MATERIALS AND METHODS: MEDLINE®, EMBASE®, Cochrane Database and gray literature were searched from January 1990 through May 2012. Included studies were matched, and measured PCA3 and comparator(s) within a cohort. No matched analyses were possible. Differences in independent performance estimates between PCA3 and comparators were computed within studies. Studies were assessed for quality using QUADAS (Quality Assessment of Diagnostic Accuracy Studies) and for strength of evidence using GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria. RESULTS: Among 1,556 publications identified, 34 observational studies were analyzed (24 addressed diagnostic accuracy and 13 addressed treatment decisions). Most studies were conducted in opportunistic cohorts of men referred for procedures and were not designed to answer key questions. Two study biases (partial verification and sampling) were addressed by analyses, allowing some conclusions to be drawn. PCA3 was more discriminatory than total prostate specific antigen increases (eg at an observed 50% specificity, summary sensitivities were 77% and 57%, respectively). Analyses indicated that this finding holds for initial and repeat biopsies, and that the markers were independent predictors. For all other biopsy decision making comparisons and associated health outcomes, strength of evidence was insufficient. For treatment decision making, strength of evidence was insufficient for all outcomes and comparators. CONCLUSIONS:
PCA3 had a higher diagnostic accuracy than total prostate specific antigen increases, but strength of evidence was low (limited confidence in effect estimates). Strength of evidence was insufficient to conclude that PCA3 testing leads to improved health outcomes. For all other outcomes and comparators, strength of evidence was insufficient.

[501]
TITULO / TITLE: - Diagnostically challenging cases: what are atypia and dysplasia?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Sanfrancesco J; Jones JS; Hansel DE
INSTITUCIÓN / INSTITUTION: - Pathology and Laboratory Medicine Institute, The Cleveland Clinic, Cleveland, OH 44195, USA.
RESUMEN / SUMMARY: - This article addresses the spectrum of atypia and dysplasia within the bladder epithelium and the diagnostic categories developed to further classify challenging lesions. In addition, the effects of inflammation, specific therapies, and instrumentation on the bladder mucosa as well as the associated difficulty in achieving the appropriate diagnosis are also discussed.

[502]
TITULO / TITLE: - Aberrant methylation and loss of CADM2 tumor suppressor expression is associated with human renal cell carcinoma tumor progression.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - He W; Li X; Xu S; Ai J; Gong Y; Gregg JL; Guan R; Qiu W; Xin D; Gingrich JR; Guo Y; Chang G
INSTITUCIÓN / INSTITUTION: - Department of Urology, Peking University First Hospital and the Institute of Urology, Peking University, No. 8, Xishiku Street, Xicheng District, Beijing 100034, China; National Urological Cancer Center, Beijing 100034, China.
RESUMEN / SUMMARY: - Cell adhesion molecules (CADMs) comprise a protein family whose functions include maintenance of cell polarity and tumor suppression. In this report, we show that the CADM2 gene is repressed in human clear renal cell carcinoma by DNA promoter hypermethylation and/or loss of heterozygosity. Moreover, the loss of CADM2 expression is associated with a higher tumor pathology stage (p<0.05). The re-expression of CADM2 in
the renal cancer cell line 786-O significantly suppressed tumor cell growth in vitro and in mouse xenografts by a G1 phase cell cycle arrest and the induction of apoptosis. Lentivirus-mediated CADM2 expression also significantly suppressed cancer cell anchorage-independent growth and invasion. Furthermore, the inhibition of endogenous CADM2 expression using siRNAs induced a tumorigenic phenotype in polarized non-tumorigenic MDCK cells. Thus, we conclude that CADM2 functions as a novel tumor suppressor and may serve as a potential therapeutic target for human renal cell carcinoma.

[503]
TÍTULO / TITLE: - Re: Inhibition of Ca(2+)-Activated Cl(-) Channel ANO1/TMEM16A Expression Suppresses Tumor Growth and Invasiveness in Human Prostate Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Atala A

[504]
TÍTULO / TITLE: - Epigenetic regulation of microRNA expression in renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - SurnameSchiffgen G; SurnameSchmidt GH; Surnamevon Rucker G; SurnameMuller GC; Surnameellinger G
INSTITUCION / INSTITUTION: - Klinik und Poliklinik fur Urologie und Kinderurologie, Universitätsklinikum Bonn, Sigmund-Freud-Strasse 25, 53105 Bonn, Germany. Electronic address: miriam.schiffgen@gmx.de.
RESUMEN / SUMMARY: - The underlying mechanisms of microRNA deregulation in cancer cells include epigenetic modifications, which play a crucial role in carcinogenesis. We demonstrate that numerous microRNAs are induced in renal cell carcinoma cell lines after treatment with inhibitors of the DNA-methyltransferase (5-aza-2'-deoxycytidine) and the histone-deacetylase (suberoylanilide hydroxamic). We provide evidence that enrichment of H3 and H3K18 acetylation at the miR-9 promoter was causative for re-expression, while DNA hypermethylation remain unchanged. Our experiments show that the treatment with the epigenetic drugs causes re-expression of silenced microRNAs with putative tumour suppressive function in ccRCC cell lines.
Exercise does not counteract the effects of a “westernized” diet on prostate cancer xenografts.

**BACKGROUND:** The relationships between diet, exercise, and prostate cancer (PCa) remain unclear. We have previously reported that a “Western” diet promotes PCa tumor growth in vivo. Presently, we report the effects of sustained aerobic exercise on PCa progression in animals fed a high-fat diet versus a standard diet. **METHODS:** Athymic mice (n = 43) were inoculated subcutaneously with human PCa (LNCaP) cells, fed ad libitum with either a high-fat or a standard diet, and randomized into forced exercising and non-exercising groups. Body weight, tumor volume, and food consumption were recorded tri-weekly. Terminal serum samples and tumor biopsies were obtained for analysis. **RESULTS:** Body weight differences were not observed between the groups over time. The high-fat diet with exercise (HF-Ex) group showed significantly increased tumor growth rate compared to all other groups (P < 0.0007). Tumor growth rate of the standard diet with exercise (Std-Ex) group was reduced significantly compared to the high-fat diet without exercise (HF-No Ex) group (P = 0.0008). Significant differences (P <= 0.012) were observed in energy consumption (kcal) between the groups over time. Exercising mice consumed significantly more kcal than non-exercising mice, and the HF-Ex group consumed significantly more than each of the other three groups (P < 0.0007). The expression levels of p27 and p21 were increased in exercising animals, while AR expression was elevated in the HF-Ex group versus the Std-Ex and HF-No Ex groups. **CONCLUSIONS:** Sustained aerobic exercise did not counteract the tumor-promotional effect of increased consumption of a high-fat diet, suggesting that diet is more influential in PCa progression than exercise. Combining exercise with a healthy diet reduced the rate of PCa progression in this model. This study may have implications for PCa risk reduction in humans.

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Background: Prostate cancer mortality has been decreasing in several high income countries and previous studies analysed the trends mostly according to geographical criteria. We aimed to identify patterns in the time trends of prostate cancer mortality across countries using a model-based approach.

Methods: Model-based clustering was used to identify patterns of variation in prostate cancer mortality (1980-2010) across 37 European, five non-European high-income countries and four leading emerging economies. We characterised the patterns observed regarding the geographical distribution and gross national income of the countries, as well as the trends observed in mortality/incidence ratios.

Results: We identified three clusters of countries with similar variation in prostate cancer mortality: pattern 1 (‘no mortality decline’), characterised by a continued increase throughout the whole period; patterns 2 (‘later mortality decline’) and 3 (‘earlier mortality decline’) depict mortality declines, starting in the late and early 1990s, respectively. These clusters are also homogeneous regarding the variation in the prostate cancer mortality/incidence ratios, while are heterogeneous with reference to the geographical region of the countries and distribution of the gross national income.

Conclusion: We provide a general model for the description and interpretation of the trends in prostate cancer mortality worldwide, based on three main patterns.


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TITULO / TITLE: - DNA Ploidy Measured on Archived Pretreatment Biopsy Material May Correlate With Prostate-Specific Antigen Recurrence After Prostate Brachytherapy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Keyes M; Macaulay C; Hayes M; Korbelik J; Morris WJ; Palcic B

INSTITUCIÓN / INSTITUTION: - Radiation Oncology, Provincial Prostate Brachytherapy Program, British Columbia Cancer Agency, Vancouver, British Columbia, Canada. Electronic address: mkeyes@bccancer.bc.ca.
PURPOSE: To explore whether DNA ploidy of prostate cancer cells determined from archived transrectal ultrasound-guided biopsy specimens correlates with disease-free survival. METHODS AND MATERIALS: Forty-seven failures and 47 controls were selected from 1006 consecutive low- and intermediate-risk patients treated with prostate 125I brachytherapy (July 1998-October 2003). Median follow-up was 7.5 years. Ten-year actuarial disease-free survival was 94.1%. Controls were matched using age, initial prostate-specific antigen level, clinical stage, Gleason score, use of hormone therapy, and follow-up (all P nonsignificant). Seventy-eight specimens were successfully processed; 27 control and 20 failure specimens contained more than 100 tumor cells were used for the final analysis. The Feulgen-Thionin stained cytology samples from archived paraffin blocks were used to determine the DNA ploidy of each tumor by measuring integrated optical densities. RESULTS: The samples were divided into diploid and aneuploid tumors. Aneuploid tumors were found in 16 of 20 of the failures (80%) and 8 of 27 controls (30%). Diploid DNA patients had a significantly lower rate of disease recurrence (P=.0086) (hazard ratio [HR] 0.256). On multivariable analysis, patients with aneuploid tumors had a higher prostate-specific antigen failure rate (HR 5.13). Additionally, those with “excellent” dosimetry (V100 >90%; D90 >144 Gy) had a significantly lower recurrence rate (HR 0.25). All patients with aneuploid tumors and dosimetry classified as “nonexcellent” (V100 <90%; D90 <144 Gy) (5 of 5) had disease recurrence, compared with 40% of patients with aneuploid tumors and “excellent” dosimetry (8 of 15). In contrast, dosimetry did not affect the outcome for diploid patients. CONCLUSIONS: Using core biopsy material from archived paraffin blocks, DNA ploidy correctly classified the majority of failures and nonfailures in this study. The results suggest that DNA ploidy can be used as a useful marker for aggressiveness of localized prostate cancer. A larger study will be necessary to further confirm our hypothesis.

[508]

TÍTULO / TITLE: - MicroRNA-205, a novel regulator of the anti-apoptotic protein Bcl2, is downregulated in prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Verdoodt B; Neid M; Vogt M; Kuhn V; Liffers ST; Palisaar RJ; Noldus J; Tannapfel A; Mirmohammadsadegh A

INSTITUCIÓN / INSTITUTION: - Institute of Pathology, Ruhr-University Bochum, D-44789 Bochum, Germany.

RESUMEN / SUMMARY: - Decreased expression of the microRNA miR-205 has been observed in multiple tumour types due to its role in the epithelial to
mesenchymal transition, which promotes metastasis. We determined the expression of miR-205 in 111 archival samples of prostate carcinoma and found it to be strongly reduced in most samples, with a median expression level of 16% in comparison to benign tissue from the same patient. Lower miR-205 expression correlated significantly with tumour size and miR-205 levels decreased with increasing Gleason score from 7ª=3+4 to 8=4+4. In addition, we describe the anti-apoptotic protein BCL2 as a target of miR-205, relevant for prostate cancer due to its role in prognosis of primary tumours and in the appearance of androgen independence. The repression of BCL2 by miR-205 was confirmed using reporter assays and western blotting. BCL2 mRNA expression in the same collective of prostate cancer tissue samples was associated with higher Gleason score and extracapsular extension of the tumour (pT3). Consistent with its anti-apoptotic target BCL2, miR-205 promoted apoptosis in prostate cancer cells in response to DNA damage by cisplatin and doxorubicin in the prostate cancer cell lines PC3 and LnCap. MiR-205 also inhibited proliferation in these cell lines.

[509]

**TITULO / TITLE:** - Comparison of oncologic outcomes after radical prostatectomy in men diagnosed with prostate cancer with PSA levels below and above 4 ng/mL.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


- Enlace al texto completo (gratuito o de pago) 1007/s00345-013-1089-0

**AUTORES / AUTHORS:** - Dariane C; Le Cossec C; Drouin SJ; Wolff B; Granger B; Mozer P; Bitker MO; Shariat SF; Cussenot O; Roupret M

**INSTITUCIÓN / INSTITUTION:** - Academic Department of Urology, Pitie-Salpetriere hospital (Assistance Publique-Hopitaux de Paris), 83, Boulevard de l'hôpital, 75013, Paris, France.

**RESUMEN / SUMMARY:** - PURPOSE: To assess whether the PSA level (threshold 4 ng/mL) is a prognostic factor in biochemical recurrence-free survival in men with prostate cancer (PCa) with an initial PSA level <10 ng/mL who underwent robotic-assisted laparoscopic radical prostatectomy (RARLP).

**METHODS:** We prospectively recruited data for consecutive patients treated by RARLP for PCa with an initial PSA level below 10 ng/mL between 2003 and 2011 at our institution. We divided the population into two groups: patients with a PSA level below 4 ng/mL (G1; n = 53) and patients with a PSA level between 4 and 10 ng/mL (G2; n = 371). Biochemical recurrence was defined as a single increase in PSA greater than 0.2 ng/mL after surgery. Multivariate analysis was used to assess prognostic factors of recurrence-free survival. RESULTS: Overall, 424 patients were included, and the median age was 62 (58-67) years.
The median PSA was 5.8 ng/mL (4.8-7.7 ng/mL). Overall, 6 patients from G1 and 34 patients from G2 experienced a biochemical recurrence. Overall, the 5-year recurrence-free survival rate was 86.6%. The PSA level at diagnosis (under or over 4 ng/mL) was not significantly linked to recurrence-free survival (HR = 0.59, p = 0.25). However, positive margins and a Gleason score >7 on the specimen were significantly linked to recurrence-free survival with respective hazard ratios of 4.30 (p < 0.0001) and 6.18 (p < 0.0001), respectively. CONCLUSION: A PSA level <4 ng/mL alone appears to be obsolete as a cut-off to define a population of men likely to have indolent disease.

[510]
TÍTULO / TITLE: - A conjugated polymer-peptide hybrid system for prostate-specific antigen (PSA) detection.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1039/c3cc00280b
AUTORES / AUTHORS: - Lee K; Mandal S; Morry J; Srivannavit O; Gulari E; Kim J
INSTITUCIÓN / INSTITUTION: - Materials Science and Engineering, University of Michigan, Ann Arbor, MI 48109, USA.
RESUMEN / SUMMARY: - We developed fast and readily applicable microarray chips to detect PSA by designing a novel conjugated polymer (energy donor) and combining it with on-chip peptide synthesis. The selective cleavage of a probing peptide labelled with a dye or a quencher (energy acceptor) produced a fluorescence sensory signal via fluorescent energy resonance transfer (FRET).

[511]
TÍTULO / TITLE: - The Burden of Urinary Incontinence and Urinary Bother Among Elderly Prostate Cancer Survivors.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1016/j.eururo.2013.03.041
AUTORES / AUTHORS: - Kopp RP; Marshall LM; Wang PY; Bauer DC; Barrett-Connor E; Parsons JK
INSTITUCIÓN / INSTITUTION: - Division of Urologic Oncology, UC San Diego Moores Cancer Center, and Division of Urology, San Diego Veterans Affairs Medical Center, University of California, San Diego, La Jolla, CA, USA.
RESUMEN / SUMMARY: - BACKGROUND: Data describing urinary health in elderly, community-dwelling prostate cancer (PCa) survivors are limited. OBJECTIVE: To elucidate the prevalence of lower urinary tract symptoms, urinary bother, and incontinence in elderly PCa survivors compared with peers without PCa. DESIGN, SETTING, AND PARTICIPANTS: A cross-sectional analysis of 5990 participants in the Osteoporotic Fractures in Men Research Group, a cohort study of community-dwelling men >/=65 yr. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: We characterized urinary health using self-reported urinary incontinence and the American Urological Association Symptom Index (AUA-SI). We compared urinary health measures according to type of PCa treatment in men with PCa and men without PCa using multivariate log-binomial regression to generate prevalence ratios (PRs). RESULTS AND LIMITATIONS: At baseline, 706 men (12%) reported a history of PCa, with a mean time since diagnosis of 6.3 yr. Of these men, 426 (60%) reported urinary incontinence. In adjusted analyses, observation (PR: 2.11; 95% confidence interval [CI], 1.22-3.65; p=0.007), surgery (PR: 4.41; 95% CI, 3.79-5.13; p<0.0001), radiation therapy (PR: 1.49; 95% CI, 1.06-2.08; p=0.02), and androgen-deprivation therapy (ADT) (PR: 2.02; 95% CI, 1.31-3.13; p=0.002) were each associated with daily incontinence. Daily incontinence risk increased with time since diagnosis independently of age. Observation (PR: 1.33; 95% CI, 1.00-1.78; p=0.05), surgery (PR: 1.25; 95% CI, 1.10-1.42; p=0.0008), and ADT (PR: 1.50; 95% CI, 1.26-1.79; p<0.0001) were associated with increased AUA-SI bother scores. Cancer stage and use of adjuvant or salvage therapies were not available for analysis. CONCLUSIONS: Compared with their peers without PCa, elderly PCa survivors had a two-fold to five-fold greater prevalence of urinary incontinence, which rose with increasing survivorship duration. Observation, surgery, and ADT were each associated with increased urinary bother. These data suggest a substantially greater burden of urinary health problems among elderly PCa survivors than previously recognized.

[512]
TÍTULO / TITLE: - Combined proteome and transcriptome analyses for the discovery of urinary biomarkers for urothelial carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Shimwell NJ; Bryan RT; Wei W; James ND; Cheng KK; Zeegers MP; Johnson PJ; Martin A; Ward DG
INSTITUCIÓN / INSTITUTION: - School of Cancer Sciences, University of Birmingham, Birmingham B15 2TT, UK.

388
RESUMEN / SUMMARY: - Background: Proteomic discovery of cancer biomarkers in body fluids is challenging because of their low abundance in a complex background. Altered gene expression in tumors may not reflect protein levels in body fluids. We have tested combining gene expression profiling of tumors with proteomic analysis of cancer cell line secretomes as a strategy to discover urinary biomarkers for bladder cancer. Methods: We used shotgun proteomics to identify proteins secreted by three bladder cancer cell lines. Secreted proteins with high mRNA levels in bladder tumors relative to normal urothelium were assayed by ELISA in urine samples from 642 patients. Results: Midkine and HAI-1 were significantly increased in bladder cancer patients, with the highest levels in invasive disease (area under the receiver operating characteristic curve 0.89 vs non-cancer). The urinary concentration of both proteins was too high to be explained by bladder cancer associated haematuria and most likely arises by direct tumor secretion. Conclusions: This ‘dual-omic’ strategy identified tumor secreted proteins whose urine concentrations are increased significantly by bladder cancer. Combined secretome-transcriptome analysis may be more useful than direct proteomic analysis of body fluids for biomarker discovery in both bladder cancer and other tumor types.

[513]

TÍTULO / TITLE: - Expression of hypoxia-inducible factor-1alpha and -2alpha in whole-mount prostate histology: relation with dynamic contrast-enhanced MRI and Gleason score.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Borren A; Groenendaal G; van der Groep P; Moman MR; Boeken Kruger AE; van der Heide UA; Jonges TN; van Diest PJ; van Vulpen M; Philippens ME

INSTITUCIÓN / INSTITUTION: - Department of Radiotherapy, University Medical Center Utrecht, Utrecht, The Netherlands. a.borren@umcutrecht.nl

RESUMEN / SUMMARY: - The aim of this study was to investigate the association between the immunohistochemical expression of hypoxia-inducible factor (HIF)-1alpha and HIF-2alpha and dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) parameters Ktrans and kep in prostate cancer. Therefore, 15 patients with biopsy-confirmed prostate cancer underwent a pre-operative 3T DCE-MRI scan. Immunohistochemical analysis of HIF-1alpha and HIF-2alpha, and of CD31 for microvessel density (MVD) was performed. Tumor areas were delineated on whole-mount histopathological sections. Nuclear HIF expression was correlated with the quantitative DCE-MRI parameters Ktrans and kep, MVD and Gleason score. HIF expression was highly heterogeneous within tumors.
and between patients. Pronounced expression of HIF-2alpha was present, while HIF-1alpha expression was more limited. Larger tumors showed higher HIF-2alpha expression (p=0.041). A correlation between HIF-2alpha and Ktrans p5th was found (r=0.30, p=0.02), but no differences in Ktrans, kep and MVD were observed for different levels of HIF expression. HIF expression was not associated with Gleason score. In conclusion, in this whole-mount prostate cancer study, larger prostate tumors showed frequently high HIF-2alpha expression, suggesting that larger tumors are clinically most relevant. However, HIF-1alpha and HIF-2alpha were not correlated with DCE-MRI parameters. Given the pronounced expression of HIF-2alpha and independence of Gleason score, HIF expression may function as a biomarker to guide boost dose prescription.

[514]
TÍTULO / TITLE: Long-term survivor of relapsed stage IV malignant rhabdoid tumor of the kidney.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Kato M; Koh K; Oshima K; Oguma E; Uchida H; Kishimoto H; Kikuchi A; Hanada R
INSTITUCIÓN / INSTITUTION: Departments of Hematology/Oncology Radiology Surgery Pathology, Saitama Children’s Medical Center, Saitama, Japan.
RESUMEN / SUMMARY: The prognosis for metastatic malignant rhabdoid tumor (MRT) is poor, and metastatic (stage IV) MRT was resistant to conventional treatment, with less than 20% of cure rate. Moreover, there have been no reports of patients who have survived relapsed stage IV MRT. Here we report a long-term survivor of relapsed MRT with lung metastasis at diagnosis. He was diagnosed as MRT of the kidney at 5-month-old. After resection of the renal tumor, he was treated with ICE (ifosfamide, carboplatin, and etoposide), total abdominal irradiation 10.8Gy and high-dose chemotherapy using thiotepa and melphalan. Six months after initial treatment, a relapse in the lung was detected, and he received chemotherapy including doxorubicin/pirarubicin for 78 weeks. He is alive at five years of follow up, without any evidence of disease. Our report suggests the important role of anthracycline in treatment of MRT.

[515]
TÍTULO / TITLE: Overexpression of RING box protein-1 (RBX1) associated with poor prognosis of non-muscle-invasive bladder transitional cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Wang W; Qiu J; Liu Z; Zeng Y; Fan J; Liu Y; Guo Y

INSTITUCIÓN / INSTITUTION: - Department of Urology, Shanghai First People’s Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; Department of Urology, The Fourth Affiliated Hospital of Nantong University (Yancheng First People’s Hospital), Jiangsu, China.

RESUMEN / SUMMARY: - BACKGROUND AND OBJECTIVE: RING box protein-1 (RBX1) is a key subunit of the ubiquitin E3 ligase Skp1/Cullin1/Rbx1/F-box protein complex. Altered expression RBX1 is shown to associate with tumorigenesis and tumor progression. This study detected RBX1 expression for association with clinical significance (such as clinicopathological data and survival of the patients) in non-muscle-invasive bladder transitional cell carcinoma (NMIBC). METHODS: A total of 70 primary NMIBC tissue specimens and 24 normal tissue specimens were recruited and analyzed immunohistochemically for expression of RBX1 protein and associated with clinicopathological data and survival of the patients. RESULTS: RBX1 was highly expressed in NMIBC, but was lowly expressed in the normal tissue. RBX1 expression was associated with high tumor grade and advanced clinical stage (P < 0.01 and P < 0.05, respectively). Moreover, patients with high RBX1 expression had shorter recurrence-free survival and progression-free survival rates (P < 0.001 and P < 0.01, respectively). Multivariate analysis demonstrated that RBX1 expression is an independent prognostic factor for tumor recurrence and progression of NMIBC (P < 0.05). CONCLUSIONS: Overexpression of RBX1 protein contributes to tumor progression and poor prognosis of NMIBC. J. Surg. Oncol. 2013;107:758-761. © 2013 Wiley Periodicals, Inc.

[516]
TÍTULO / TITLE: - 8q24 amplification is associated with Myc expression and prostate cancer progression and is an independent predictor of recurrence after radical prostatectomy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Fromont G; Godet J; Peyret A; Irani J; Celhay O; Rozet F; Cathelineau X; Cussenot O
INSTITUCIÓN / INSTITUTION: - Department of Pathology, CHU/Universite de Poitiers, 86000 Poitiers, France; Centre d’Etude et de Recherche sur les
RESUMEN / SUMMARY: - Genomic alterations affecting the 8q24 region are frequent in prostate cancer. Together with the oncogene MYC, other genes located in the surrounding of the amplified region could also be candidate targets. Tissue microarrays were constructed with prostate cancer tissues from (1) a case-control population of patients treated by radical prostatectomy (n = 242; 121 cases with biochemical relapse matched with 121 cancers with identical clinicopathologic features but without relapse), (2) castration-resistant disease (n = 55), and (3) metastatic cancers (n = 28). Fluorescence in situ hybridization and immunohistochemistry were used on tissue microarrays and slides to analyze, respectively, the amplification status of 8q24 and protein expression of genes located at 8q24. Amplification at the MYC locus was observed in 29% of cases and was closely associated with both disease progression (from 15% in pT2 tumors to 53% in metastasis; P = .001), and Gleason score (from <3% in Gleason 6 tumors to 66% in Gleason 8 and more tumors; P < .0001). The expression of genes located at 8q24 did not correlate with the amplification status, except for the Myc protein (P = .002). MYC amplification status but not Myc protein expression was significantly predictive of biochemical recurrence after prostatectomy, together with the proliferation marker Ki-67 and independently from known prognostic factors, including TNM stage and Gleason score. The MYC amplification status could constitute a useful prognostic tool for patients treated by radical prostatectomy, particularly for those with d’Amico intermediate risk, whose clinical behavior is currently difficult to predict.

[517]

TÍTULO / TITLE: - An assessment of the shared allelic architecture between type 2 diabetes and prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Yu OH; Foulkes WD; Dastani Z; Martin RM; Eeles R; Richards JB

INSTITUCIÓN / INSTITUTION: - McGill University.

RESUMEN / SUMMARY: - Background:To determine whether the alleles that influence type 2 diabetes risk and glycemic traits also influence prostate cancer risk. Methods:We used a multiple single nucleotide polymorphisms (SNP) genotypic risk score to assess the average effect of alleles that increase type 2 diabetes risk or worsen glycemic traits on risk of prostate cancer in 19,662 prostate cancer cases and 19,715 controls from the PRACTICAL consortium
and 5,504 prostate cancer cases and 5,834 controls from the CRUK prostate cancer study. Results:Calculating the average additive effect of type 2 diabetes or glycemic trait risk alleles on prostate cancer risk using a logistic model revealed no evidence of a shared allelic architecture between type 2 diabetes, or worsened glycemic status, with prostate cancer risk (odds ratio for type 2 diabetes alleles: 1.00 (P=0.58), fasting glycemia alleles: 1.00 (P=0.67), HbA1c alleles: 1.00 (P=0.93), 2 hour OGTT alleles: 1.01 (P=0.14) and HOMA-B alleles: 0.99 (P=0.57)). Conclusions:Using genetic data from large consortia we found no evidence for a shared genetic etiology of type 2 diabetes, or glycemic risk, with prostate cancer. Impact:Our results showed that alleles influencing type 2 diabetes and related glycemic traits were not found to be associated with the risk of prostate cancer.

[518]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Sutoris K; Rakusan J; Karaskova M; Mattova J; Benes J; Nekvasil M; Jezek P; Zadinova M; Pouckova P; Vetvicka D
INSTITUCIÓN / INSTITUTION: - Charles University in Prague, Third Faculty of Medicine, Prague, Czech Republic. sutoris@gmail.com
RESUMEN / SUMMARY: - BACKGROUND: Clinically-approved anticancer photodynamic therapy (PDT) is now extensively studied for various cancer diagnoses. We focused on the treatment efficacy of topical administration of hydroxy-aluminum phthalocyanine (AlOH-PC) entrapped in liposomes against in vivo models of prostate carcinomas. MATERIALS AND METHODS: LNCaP and PC3 cells were subcutaneously injected into the right flank of athymic nude mice. Mice with grown tumours were used for in vivo efficacy studies. Firstly, we applied different doses of AlOH-PC to less aggressive LNCaP tumours to determine the effective dose. In later studies, we focused on more aggressive prostate tumours (PC3) using doses of liposomal-AlOH-PC gel formulation. Topical application of photosensitizers was followed by PDT irradiation (600-700 nm, 635 nm peak). Tumour growth was measured three times-a-week. RESULTS: Comparison of PDT of aggressive PC3 and less aggressive LNCaP prostate carcinomas showed that both tumour types are sensitive and treatable by liposomal formulation of AlOH-PC. For LNCaP tumours the efficient dose (100% experimental animals cured, n=8/8) was 4.5 mg/ml of AlOH-PC in the gel. Whereas, in the case of PC3 carcinosomas, a dose of 4 mg/ml significantly postponed tumour growth, but no animals were cured (n=0/8); a sufficient curative dose (100% mice cured, n=8/8) was 6 mg/ml of AlOH-PC in the gel.
CONCLUSION: Liposomal ALOH-PC gel has potential for effective PDT of prostate carcinomas.

[519]
**TÍTULO / TITLE:** - Re: an updated prostate cancer staging nomogram (partin tables) based on cases from 2006 to 2011.
**RESUMEN / SUMMARY:** - [Link to its Summary](https://doi.org/10.1016/j.juro.2012.12.069)
**AUTORES / AUTHORS:** - Taneja SS

[520]
**TÍTULO / TITLE:** - Expanded Criteria to Identify Men Eligible for Active Surveillance of Low-Risk Prostate Cancer at Johns Hopkins: A Preliminary Analysis.
**RESUMEN / SUMMARY:** - [Link to its Summary](https://doi.org/10.1016/j.juro.2013.05.015)
**AUTORES / AUTHORS:** - Reese AC; Landis P; Han M; Epstein JI; Carter HB
**INSTITUCIÓN / INSTITUTION:** - The James Buchanan Brady Urological Institute, Johns Hopkins University, Baltimore, MD. Electronic address: areese11@jhmi.edu.
**RESUMEN / SUMMARY:** - PURPOSE: The following eligibility criteria are used to enroll patients in active surveillance (AS) at Johns Hopkins: clinical stage T1, PSA density < 0.15, biopsy Gleason score <= 6, <=2 positive biopsy cores, and <= 50% involvement of any biopsy core. We hypothesized that these criteria may be excessively strict, thereby precluding many men from AS. MATERIALS AND METHODS: We studied pathological outcomes in men treated between 1995 and 2012 with radical prostatectomy (RP) who met >= 4 of 5 AS criteria. Outcomes included a definition of significant tumor (pathological Gleason >= 7 or non-organ confined). Rates of adverse pathology were compared between men meeting all versus 4 of 5 AS criteria. RESULTS: Of 8261 men, 1890 (22.9%) met all AS eligibility criteria and 2133 (25.8%) met 4 of 5 criteria. Men exceeding PSA density and biopsy Gleason criteria were at increased risk of adverse pathological outcomes. Clinical stage > T1 was not associated with adverse pathology. Men with clinical stage T2 lesions, <=3 positive biopsy cores, and < 60% core involvement were at comparable risk of significant tumors to men meeting all AS criteria. CONCLUSIONS: PSA density > 0.15 ng/ml and biopsy Gleason score >= 7 are strongly associated with...
adverse pathology at RP. Our findings suggest expanding AS criteria to include men with clinical stage T2 lesions and a greater number of positive biopsy cores of low grade. Based on these preliminary findings, we are in the process of reassessing AS eligibility criteria using more detailed pathological analysis.

[521]

TÍTULO / TITLE: - Crosstalk among dietary polyunsaturated fatty acids, urolithiasis, chronic inflammation, and urinary tract tumor risk.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Eynard AR; Navarro A
INSTITUCIÓN / INSTITUTION: - Instituto de Biología Celular, INICSA, Cordoba, Argentina. Electronic address: aeynard@gmail.com.

RESUMEN / SUMMARY: - Based on a consistent bulk of experimental and epidemiologic works, we proposed that abnormal metabolism and/or dietary deprivation of essential polyunsaturated fatty acids by inducing a chronic and subclinical essential fatty acid deficiency (EFAD) in urothelial cell membranes may enhance the risk for urinary tract tumor (UTT) development. This threat may be enhanced by the unusual fact that the fatty-acid profile of the normal urothelium is similar to that reported in EFAD. The risk for UTT may be worsened when coexisting with a low-grade chronic inflammation (LGCI) state induced by urolithiasis or disbalance management of peroxides, free radical molecules, and their quenchers. There is cumulative evidence linking the LGCI of the urinary tract mucosa, calculi, and UTT, due to the long-standing release of promitotic, promutagen, and pro-inflammatory antiapoptotic cytokines in these conditions. The dual role played by pro- and anti-inflammatory eicosanoids and bioactive lipids, cytokines, and the disbalance of lipid peroxidation is discussed, concluding that the moderate, long-standing consumption or dietary supplementation of omega-3 PUFAs may improve the chances of avoiding UTT development.

[522]

TÍTULO / TITLE: - Strategies for optimizing bacillus Calmette-Guerin.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Shah JB; Kamat AM
INSTITUCIÓN / INSTITUTION: - Department of Urology, MD Anderson Cancer Center, Houston, TX 77030, USA.

RESUMEN / SUMMARY: - For treating patients with superficial bladder cancer and a moderate-to-high risk of tumor recurrence or progression, intravesical BCG has been the key development of the last generation. However, BCG has also brought with it a novel set of challenges. An understanding of when, to whom, and how BCG should be given is critical if optimal outcomes are to be achieved. This article the authors reviews the role that BCG has played in the management of bladder cancer over the last several decades and discusses specific approaches to optimize BCG. It focuses on selection and technical strategies.

TÍTULO / TITLE: - Screening for prostate cancer in New Zealand general practice.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Zuzana O; Ross L; Fraser H; Charis B; Alistair S; Leanne T; Michael H; Peter G

INSTITUCIÓN / INSTITUTION: - PhD student, Waikato Clinical School, University of Auckland, Hamilton, New Zealand.

RESUMEN / SUMMARY: - OBJECTIVE: To ascertain the rates and patterns of prostate-specific antigen (PSA) screening in New Zealand men. METHODS: The study population included 35,958 men aged 40+ years, with no prior diagnosis of prostate cancer, enrolled in 31 general practices in the Midland Cancer Network Region of New Zealand in 2010. Computerized practice records were searched for information, including reasons for testing, for men with elevated PSA test results in 2010. PSA results for 2007-2010 were obtained from community laboratories. Screened men were identified and screening rates calculated by age. RESULTS: Of 9344 men who underwent one or more PSA tests in 2010, 84.9% were classified as having been screened. The overall screening rate was 22.1%, with 24.4% of men aged 70+ years screened. Elevated PSA levels were found in 2.1% of screened men. Of the men screened in 2010, 57.3% had had a screening test in the previous three years. CONCLUSIONS: General practitioners in New Zealand commonly screen men (including those aged 70+) for prostate cancer, despite the lack of trial evidence that these men would benefit from screening. The value of annual PSA testing in men with previous normal PSA levels is unproven. Longer intervals between tests would be appropriate.
TÍTULO / TITLE: Stage I testicular seminoma: a SEER analysis of contemporary adjuvant radiotherapy trends.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Thong AE; Lichtensztajn DY; Almario L; Ingels A; Gomez SL; Gonzalgo ML
INSTITUCIÓN / INSTITUTION: Department of Urology, Stanford University School of Medicine, Stanford, California.

PURPOSE: Patients with clinical stage I testicular seminoma have historically been treated with adjuvant radiotherapy (RT) in the United States. However, nearly 80% of patients on surveillance will not relapse and even with relapse, salvage rates approach 100%. It remains unclear how practice patterns have changed with recently accumulating evidence and changes in guidelines. We evaluated, in a population-based setting, contemporary trends and factors that may affect utilization of adjuvant RT.
MATERIALS AND METHODS: A total of 8,151 men from 2000 to 2009 diagnosed with stage I testicular seminoma were identified in the national Surveillance, Epidemiology, and End Results (SEER) registry. A multivariate regression model was constructed to analyze the association of year, age, race, socioeconomic status, SEER region, pathologic stage, and tumor size with administration of adjuvant RT.
RESULTS: Utilization of adjuvant RT significantly decreased from 2000 to 2009. In 2000, 74.7% of patients received radiation, compared with only 37.7% of patients in 2009 (p<0.0001). Later year of diagnosis was significantly associated with decreased odds of receiving adjuvant RT (p<0.0001, 2000-2005 vs. 2006-2009, Odds ratio (OR) 0.40, 95% CI 0.36-0.44). Men older than 35 years (p<0.0002, OR 1.20, 95% CI 1.09-1.32) and men in the highest socioeconomic index quartile (p<0.0001, OR 1.34, 95% CI 1.16-1.54) were more likely to receive adjuvant RT.
CONCLUSIONS: Utilization of adjuvant RT for clinical stage I testicular seminoma has decreased significantly in the last decade. Older age and higher socioeconomic status were associated with higher rates of adjuvant RT.

TÍTULO / TITLE: Technology diffusion and diagnostic testing for prostate cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** Schroeck FR; Kaufman SR; Jacobs BL; Skolarus TA; Miller DC; Weizer AZ; Montgomery JS; Wei JT; Shahinian VB; Hollenbeck BK

**INSTITUCIÓN / INSTITUTION:** Division of Health Services Research, University of Michigan, Ann Arbor, MI; Division of Urologic Oncology, University of Michigan, Ann Arbor, MI.

**RESUMEN / SUMMARY:**

**PURPOSE:** While the dissemination of robotic prostatectomy and intensity-modulated radiotherapy (IMRT) may fuel increased use of prostatectomy and radiotherapy, these new technologies may also have spillover effects related to diagnostic testing for prostate cancer. Therefore, we examined the association of regional technology penetration with receipt of prostate specific antigen (PSA) testing and prostate biopsy.

**METHODS:** In this retrospective cohort study, we included 117,857 men age 66 and older from the 5% sample of Medicare beneficiaries living in the Surveillance Epidemiology and End Results (SEER) areas from 2003 - 2007. Regional technology penetration was measured as the number of providers performing robotic prostatectomy or IMRT per population in a healthcare market (i.e., hospital referral region). We assessed the association of technology penetration with rates of PSA testing and prostate biopsy with generalized estimating equations.

**RESULTS:** High technology penetration was associated with increased rates of PSA testing (442 versus 425 per 1,000 person-years, p<0.01) and similar rates of prostate biopsy (10.1 versus 9.9 per 1,000 person-years, p=0.69). The impact of technology penetration on PSA testing and prostate biopsy was much smaller than the effect of age, race, and comorbidity (e.g., PSA testing rate per 1,000 person-years: 485 versus 373 for men with only one versus 3+ co-morbid conditions, p<0.01).

**CONCLUSIONS:** Increased technology penetration was associated with slightly higher rates of PSA testing and no change in prostate biopsy rates. Collectively, our findings temper concerns that adoption of new technology accelerates diagnostic testing for prostate cancer.

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**AUTORES / AUTHORS:** Mengual L; Lozano JJ; Ingelmo-Torres M; Gazquez C; Ribal MJ; Alcaraz A

**INSTITUCIÓN / INSTITUTION:** Laboratory and Department of Urology, Universitat de Barcelona, España.

**RESUMEN / SUMMARY:** Current standard methods used to detect and monitor bladder urothelial cell carcinoma (UCC) are invasive or have low sensitivity. The
incorporation into clinical practice of a non-invasive tool for UCC assessment would enormously improve patients’ quality of life and outcome. This study aimed to examine the microRNA (miRNA) expression profiles in urines of UCC patients in order to develop a non-invasive accurate and reliable tool to diagnose and provide information on the aggressiveness of the tumour. We performed a global miRNA expression profiling analysis of the urinary cells from 40 UCC patients and controls using TaqMan® Human MicroRNA Array followed by validation of 22 selected potentially diagnostic and prognostic miRNAs in a separate cohort of 277 samples using a miRCURY LNA™ qPCR system. miRNA-based signatures were developed by multivariate logistic regression analysis and internally cross-validated. In the initial cohort of patients, we identified 40 and 30 aberrantly expressed miRNA in UCC compared to control urines and in high compared to low grade tumours, respectively. Quantification of 22 key miRNAs in an independent cohort resulted in the identification of a six miRNA diagnostic signature with a sensitivity of 84.8% and specificity of 86.5% (AUC=0.92) and a two miRNA prognostic model with a sensitivity of 84.95% and a specificity of 74.14% (AUC=0.83). Internal cross-validation analysis confirmed the accuracy rates of both models, reinforcing the strength of our findings. Although the data needs to be externally validated, miRNA analysis in urine appears to be a valuable tool for the non-invasive assessment of UCC. © 2013 Wiley Periodicals, Inc.

[527]

TÍTULO / TITLE: - Knockout of the tetraspanin Cd9 in the TRAMP model of de novo prostate cancer increases spontaneous metastases in an organ-specific manner.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Copeland BT; Bowman MJ; Boucheix C; Ashman LK

INSTITUCIÓN / INSTITUTION: - School of Biomedical Sciences and Pharmacy, University of Newcastle and Cancer Research Program, Hunter Medical Research Institute, Newcastle, Australia.

RESUMEN / SUMMARY: - Prostate cancer is an extremely heterogeneous disease; patients that do progress to late-stage metastatic prostate cancer have limited treatment options, mostly palliative. Molecules involved in the metastatic cascade may prove beneficial in stratifying patients to assign appropriate treatment modalities and may also prove to be therapeutic antimitastatic targets. The tetraspanin group of molecules are integral membrane proteins that associate with motility-related proteins such as integrins. Clinical studies have mostly shown that reduced expression levels of the tetraspanin CD9 are correlated with tumour progression in a range of
cancers. Furthermore, functional studies have shown CD9 to be involved in cell motility and adhesion and that it may influence metastasis. The effects of endogenous CD9 on prostate cancer initiation and progression were analysed by crossing a Cd9-/- (KO) murine model with a model of de novo developing and spontaneously metastasising prostate cancer, namely the transgenic adenocarcinoma of mouse prostate model. Our study demonstrates for the first time that ablation of Cd9 had no detectable effect on de novo primary tumour onset, but did significantly increase metastasis to the liver but not the lungs.

[528] 
**TÍTULO / TITLE:** Congenital malformations and testicular germ cell tumors. 
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary 
**AUTORES / AUTHORS:** Trabert B; Zugna D; Richiardi L; McGlynn KA; Akre O 
**INSTITUCIÓN / INSTITUTION:** Hormonal and Reproductive Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD. 
**RESUMEN / SUMMARY:** Cryptorchidism is one of the few known risk factors for testicular germ cell tumors (TGCT). It has been postulated that other congenital malformations, in particular hypospadias, are also associated with increased risk; however, associations with birth defects have not been extensively studied. Using Swedish population-based registries we evaluated the relationship between birth defects and risk of TGCT. TGCT cases (n = 6,593) diagnosed between 15 and 65 years of age were identified from the Swedish Cancer Registry between 1964 and 2008. Five controls per case were randomly selected from the population register and matched on birth year and birth county. Congenital malformations were identified via linkage with the Hospital Discharge Register. Odds ratios (ORs) and 95% confidence intervals (CIs) for the association between each group of malformations and TGCT were estimated using conditional logistic regression. In addition to the expected association between cryptorchidism and TGCT risk [OR (95% CI): 3.18 (2.50-4.04)], hypospadias [2.41 (1.27-4.57)], inguinal hernia [1.37 (1.11-1.68)] and other genital malformations [2.19 (1.17-4.10)] were associated with an increased risk of TGCT. Mutual adjustment for cryptorchidism, hypospadias, inguinal hernia and other genital malformations did not appreciably change the associations (ORs: 3.16, 2.25, 1.30 and 1.90, respectively). The other (nongenital) malformations evaluated were not associated with TGCT. These data suggest that developmental urogenital abnormalities, specifically cryptorchidism, hypospadias and inguinal hernia, are associated with an increased risk of TGCT, further supporting the hypothesis that prenatal exposure(s) related to proper genital development are related to this tumor.
TÍTULO / TITLE: - Abrupt Intracardiac Growth of a Wilms Tumor.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Gortani G; Anzini M; Berton E; Rabusin M; Murru F; Benettoni A
INSTITUCIÓN / INSTITUTION: - Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy.

TÍTULO / TITLE: - Blocking mtDNA Replication Upregulates the Expression of Stemness-related Genes in Prostate Cancer Cell Lines.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Liu Y; Wu X; Li X; Kvalheim G; Axcrona U; Axcrona K; Suo Z
INSTITUCIÓN / INSTITUTION: - Department of Urology, The Norwegian Radium Hospital, Oslo University Hospital , Oslo, Norway.
RESUMEN / SUMMARY: - Abstract Ethidium bromide (EtBr) is an intercalating agent, which binds tightly to mitochondrial DNA (mtDNA) during replication, and so blocks the function of mitochondria. EtBr inserts itself between the stacked bases in double-stranded DNA and specifically inhibits mtDNA transcription and replication by deleting RNA primers required for initiating mtDNA replication. In this study, the authors wanted to examine whether blocking mtDNA replication with EtBr could change the expression of stemness genes and the expression of the immuneregulator B7-H3 in prostate cancer cell lines in vitro. Both PC-3 and DU145 prostate cancer cell lines were treated with 50 and 500 ng/mL of EtBr for 2 weeks. There was no difference in growth between EtBr-treated and control cells after 1 week. A slightly slower growth was observed for both cell lines during the second week of culture with EtBr compared to controls. After 2 weeks of culture with EtBr both cell lines showed increased expression of the stemness-related genes ABCG2, Oct3/4, Nanog1/Nanogp8, and CD44. Concomitantly, a dose-dependent increase of B7-H3 protein expression in both cell lines was identified and verified by both flow cytometry and immunocytochemistry. In conclusion, blocking mtDNA replication by EtBr
induces increased expression of stemness genes, such as Oct3/4, Nanog, CD44, and ABCG2, in addition to the immune regulator B7-H3 in PC-3 and DU145 prostate cancer cell lines. The findings indicate that mitochondrial function may be associated with stemness of cancer cells and/or maintenance of a cancer stem cell phenotype. The finding of increased B7-H3 expression may be associated with the immunosuppression of cancer cells.

[531]

TÍTULO / TITLE: - Re: multidisciplinary care and pursuit of active surveillance in low-risk prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Taneja SS

[532]

TÍTULO / TITLE: - Prostate stereotactic ablative body radiotherapy using a standard linear accelerator: Toxicity, biochemical, and pathological outcomes.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Loblaw A; Cheung P; D’Alimonte L; Deabreu A; Mamedov A; Zhang L; Tang C; Quon H; Jain S; Pang G; Nam R

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Toronto, Canada; Department of Health Policy, Measurement and Evaluation, University of Toronto, Canada; Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Western Australia, Australia. Electronic address: andrew.loblaw@sunnybrook.ca.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: Biological dose escalation through stereotactic ablative radiotherapy (SABR) holds promise of improved patient convenience, system capacity and tumor control with decreased cost and side effects. The objectives are to report the toxicities, biochemical and pathologic outcomes of this prospective study. MATERIALS AND METHODS: A phase I/II study was performed where low risk localized prostate cancer received SABR 35Gy in 5 fractions, once weekly on standard linear accelerators. Common Terminology Criteria for Adverse Events v3.0 and Radiation Therapy Oncology Group late morbidity scores were used to assess acute and late toxicities, respectively. Biochemical control (BC) was defined by
the Phoenix definition. RESULTS: As of May 2012, 84 patients have completed treatment with a median follow-up of 55 months (range 13-68 months). Median age was 67 years and median PSA was 5.3 ng/ml. The following toxicities were observed: acute grade 3+: 0% gastrointestinal (GI), 1% genitourinary (GU), 0% fatigue; late grade 3+: 1% GI, 1% GU. Ninety-six percent were biopsy negative post-treatment. The 5-year BC was 98%. CONCLUSIONS: This novel technique employing standard linear accelerators to deliver an extreme hypofractionated schedule of radiotherapy is feasible, well tolerated and shows excellent pathologic and biochemical control.

[533]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kearns B; Lloyd Jones M; Stevenson M; Littlewood C
INSTITUCIÓN / INSTITUTION: - School of Health and Related Research, University of Sheffield, Sheffield, S1 4DA, UK, b.kearns@sheffield.ac.uk.
RESUMEN / SUMMARY: - The National Institute for Health and Clinical Excellence (NICE) invited the manufacturer of cabazitaxel (Jevtana®), sanofi-aventis, UK to submit evidence of its clinical and cost effectiveness for the second-line treatment of metastatic hormone-refractory prostate cancer (mHRPC). The School of Health and Related Research Technology Appraisal Group (ScHARR-TAG) at the University of Sheffield was commissioned to act as the independent Evidence Review Group (ERG). The ERG produced a critical review of the evidence for the clinical and cost effectiveness of the technology based upon the manufacturer’s submission to NICE. Clinical evidence was derived from a multinational randomized open-label phase III trial of cabazitaxel plus prednisone or prednisolone in men with mHRPC that had progressed during or following treatment with docetaxel. The comparator was mitoxantrone plus prednisone or prednisolone. Use of cabazitaxel was associated with a statistically significant improvement in overall survival, median progression-free survival and time to tumour progression. However, it was also associated with an increased incidence of adverse events such as neutropenia. Utility data were based on interim results from the early access programme for cabazitaxel. Data were only available for a small number of patients with stable disease, resulting in great uncertainty as to the effect of cabazitaxel on quality of life. For their economic evaluation, the manufacturer estimated that the use of cabazitaxel was associated with an incremental cost of pound74,908 per QALY gained.
However, the ERG disagreed with the manufacturer over two key methodological points. The first concerned modelling and extrapolating survival; the second point was concerned with the choice of patient population. The ERG altered the manufacturer’s evaluation to take into account these two points of disagreement. The resulting cost per QALY gained was pound82,950. The NICE Appraisal Committee believed the analysis presented by the ERG to be more plausible, and likely to be an underestimate of the cost per QALY. They concluded that whilst the clinical effectiveness of cabazitaxel had been proven, it was not likely to represent a cost-effective use of NHS resources and so its use could not be recommended.

[534]

**TÍTULO / TITLE:** Prolyl carboxypeptidase: a forgotten kidney angiotensinase.

Focus on “Identification of prolyl carboxypeptidase as an alternative enzyme for processing of renal angiotensin II using mass spectrometry”.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Carlos Q Velez J

**INSTITUCIÓN / INSTITUTION:** Division of Nephrology, Department of Medicine, Medical University of South Carolina, Charleston, South Carolina.

[535]

**TÍTULO / TITLE:** Are bisphosphonates an indispensable tool in the era of targeted therapy for renal cell carcinoma and bone metastases?

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Keizman D; Ish-Shalom M; Maimon N; Gottfried M

**INSTITUCIÓN / INSTITUTION:** Genitourinary Oncology Service, Institute of Oncology, Meir Medical Center, Sackler School of Medicine, Tel Aviv University, Tchernichovsky 59, 44281, Kfar-Saba, Israel, danielkeizman@gmail.com.

**RESUMEN / SUMMARY:** One third of patients with metastatic renal cell carcinoma (RCC) suffer from bone metastases. Skeletal involvement in RCC is associated with the occurrence of skeletal-related events, and may negatively impact on the outcome of patients treated with systemic therapies. In patients with RCC and bone metastases, therapies that inhibit osteoclasts, as bisphosphonates and denosumab, are used as adjunct to systemic targeted therapies to prevent skeletal-related events. Data suggest that they may also
improve the outcome of systemic targeted therapies. Herein we review the
preclinical and clinical data on their use, as well as remaining open questions.

[536]
TÍTULO / TITLE: - Nonlinear system identification for prostate cancer and
optimality of intermittent androgen suppression therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.mbs.2013.04.007
AUTORES / AUTHORS: - Suzuki T; Aihara K
INSTITUCIÓN / INSTITUTION: - Department of Mathematical Informatics, Graduate
School of Information Science and Technology, The University of Tokyo, 7-3-1
Hongo, Bunkyo-ku, Tokyo 113-8656, Japan.
RESUMEN / SUMMARY: - These days prostate cancer is one of the most common
types of malignant neoplasm in men. Androgen ablation therapy (hormone
therapy) has been shown to be effective for advanced prostate cancer.
However, continuous hormone therapy often causes recurrence. This results
from the progression of androgen-dependent cancer cells to androgen-
independent cancer cells during the continuous hormone therapy. One possible
method to prevent the progression to the androgen-independent state is
intermittent androgen suppression (IAS) therapy, which ceases dosing
intermittently. In this paper, we propose two methods to estimate the dynamics
of prostate cancer, and investigate the IAS therapy from the viewpoint of
optimality. The two methods that we propose for dynamics estimation are a
variational Bayesian method for a piecewise affine (PWA) system and a
Gaussian process regression method. We apply the proposed methods to real
clinical data and compare their predictive performances. Then, using the
estimated dynamics of prostate cancer, we observe how prostate cancer
behaves for various dosing schedules. It can be seen that the conventional IAS
therapy is a way of imposing high cost for dosing while keeping the prostate
cancer in a safe state. We would like to dedicate this paper to the memory of
Professor Luigi M. Ricciardi.

[537]
TÍTULO / TITLE: - CDK Inhibitors Induce Mitochondria-Mediated Apoptosis
Through The Activation Of Polyamine Catabolic Pathway in LNCaP, DU145 and
PC3 Prostate Cancer Cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Androgen signaling is critical in prostate cancer development and progression. The co-existence of hormone responsive and irresponsive cells due to functional androgen receptor (AR) in prostate gland is the major obstacle in prostate cancer therapy models. Targeting aberrant cell cycle by novel cell cycle blocking agents is a promising strategy to treat various types of malignancies. Purvalanol and roscovitine are cyclin dependent kinase (CDK) inhibitors able to activate apoptotic cell death by inducing cell cycle arrest at G1/S and G2/M phases in cancer cells. Polyamines are unique cationic amine derivatives involved in the regulation of cell proliferation. Although the elevated intracellular level of polyamines (putrescine, spermidine and spermine) is typical for prostate gland, abnormal regulation of polyamine metabolism might result in rapid cell proliferation and, thus in prostate cancer progression. Therefore, treatment with drug-induced depletion of intracellular polyamine levels through the activated polyamine catabolism is critical to achieve successful strategies for prostate cancer. In this study we aimed to investigate the apoptotic efficiency of CDK inhibitors in three prostate cancer cell lines (LNCaP, DU145 and PC3), showing different AR expression profile. We found that both purvalanol and roscovitine were able to induce apoptosis at moderate cytotoxic concentrations by decreasing mitochondria membrane potential. The apoptotic effect of both CDK inhibitors was due to activation of caspases by modulating Bcl-2 family members. The efficiency of drugs was quite similar on the three prostate cell lines used in this study. However, DU145 cells were found the least sensitive against CDK inhibitors while purvalanol was more potent than roscovitine. Similarly to classical chemotherapeutic agents, both drugs could up-regulate polyamine catabolic enzymes (SSAT, SMO and PAO) in cell type dependent manner. Transient silencing of SSAT and/or inhibition of PAO/SMO with MDL72527 prevented CDK inhibitors-induced apoptotic cell death in DU145 and PC3 cells. Although roscovitine was less effective in DU145 cells, pre-treatment with alpha-difluoromethylornithine (DFMO), an inhibitor of ODC, enhanced the roscovitine-induced apoptotic cell death through the cleavage of caspase-9 and caspase-3. Therefore, we conclude that polyamine catabolism might have essential role in the cellular responses against CDK inhibitors in different androgen-responsive or irresponsive prostate cancer cells.
Patterns of Bone Mineral Density Testing in Men Receiving Androgen Deprivation for Prostate Cancer.

**RESUMEN / SUMMARY:**
Practice guidelines recommend bone mineral density (BMD) monitoring for men on androgen deprivation therapy (ADT) for prostate cancer, but single center studies suggest this is underutilized. OBJECTIVE: We examined determinants of BMD testing in men receiving ADT in a large population-based cohort of men with prostate cancer. DESIGN: Retrospective cohort study. PARTICIPANTS: We used the Surveillance, Epidemiology and End-Results (SEER)-Medicare database to identify 84,036 men with prostate cancer initiating ADT from 1996 through 2008. MAIN MEASURES: Rates of BMD testing within the period 12 months prior to 3 months after initiation of ADT were assessed and compared to matched controls without cancer and to men with prostate cancer not receiving ADT. A logistic regression model was performed predicting use of BMD testing, adjusted for patient demographics, indications for ADT use, year of diagnosis and specialty of the physician involved in the care of the patient. KEY RESULTS: Rates of BMD testing increased steadily over time in men receiving ADT, diverging from the control groups such that by 2008, 11.5 % of men were receiving BMD testing versus 4.4 % in men with prostate cancer not on ADT and 3.8 % in the non-cancer controls. In the logistic regression model, year of diagnosis, race/ethnicity, indications for ADT use and geographic region were significant predictors of BMD testing. Patients with only a urologist involved in their care were significantly less likely to receive BMD testing as compared to those with both a urologist and a primary care physician (PCP) (odds ratio 0.71, 95 % confidence interval 0.64-0.80). CONCLUSIONS: There has been a sharp increase in rates of BMD testing among men receiving ADT for prostate cancer over time, beyond rates noted in contemporaneous controls. Absolute rates of BMD testing remain low, however, but are higher in men who have a PCP involved in their care.

A phase II study of gemcitabine and oxaliplatin in advanced transitional cell carcinoma of the bladder.

**RESUMEN / SUMMARY:**
[539]
Cisplatin-based chemotherapy is recommended for use as first-line treatment for patients with advanced transitional cell carcinoma of the bladder. Unfortunately, 30-50% of patients are ineligible for cisplatin due to renal insufficiency. Oxaliplatin is a less nephrotoxic platin which can be used for patients with impaired renal function. We carried out a phase II study of gemcitabine (1,200 mg/m²) in combination with oxaliplatin (100 mg/m²) given on days 1 and 14 every 28 days (GEMOX) in predominantly cisplatin-'unfit' stage IV transitional cell bladder cancer patients to determine whether this combination exhibited a clinical activity profile similar to cisplatin plus gemcitabine. Eighteen patients with a median GFR of 49 ml/min were enrolled. GEMOX treatment led to a 36% response rate in assessable patients. Median progression-free survival was 4.9 months, with a median overall survival (OS) of 10.4 months and a one-year survival rate of 44.4%. GEMOX in bladder cancer patients exhibited a tolerable side effects profile, with thrombocytopenia as the most frequent grade ¾ toxicity. These findings suggest that GEMOX is an active combination in advanced bladder cancer patients with reduced renal function.
BACKGROUND: Patients with a cortical small (≤4 cm) renal mass often are not candidates for or choose not to undergo surgery. The optimal management strategy for such patients is unclear. METHODS: A decision-analytic Markov model was developed from the perspective of a third party payer to compare the quality-adjusted life expectancy and lifetime costs for 67-year-old patients with a small renal mass undergoing premanagement decision biopsy, immediate percutaneous radiofrequency ablation or percutaneous cryoablation (without premanagement biopsy), or active surveillance with serial imaging and subsequent ablation if needed. RESULTS: The dominant strategy (most effective and least costly) was active surveillance with subsequent cryoablation if needed. On a quality-adjusted and discounted basis, immediate cryoablation resulted in a similar life expectancy (3 days fewer) but cost $3,010 more. This result was sensitive to the relative rate of progression to metastatic disease. Strategies that employed radiofrequency ablation had decreased quality-adjusted life expectancies (82-87 days fewer than the dominant strategy) and higher costs ($3,231-$6,398 more). CONCLUSIONS: Active surveillance with delayed percutaneous cryoablation, if needed, may be a safe and cost-effective alternative to immediate cryoablation. The uncertainty in the relative long-term rate of progression to metastatic disease in patients managed with active surveillance versus immediate cryoablation needs to be weighed against the higher cost of immediate cryoablation. A randomized trial is needed directly to evaluate the nonsurgical management of patients with a small renal mass, and could be limited to the most promising strategies identified in this analysis.

[542] TÍTULO / TITLE: Transperitoneal Laparoscopic Excision of Primary Seminal Vesicle Benign Tumors: Surgical Techniques and Follow-up Outcomes.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Zhang DX; Li Y; Li XG; Zhu X; Teng JF; Wang K; Wang JK; Chen L; Cui XG; Xu DF
OBJECTIVE: To assess the feasibility, safety, and efficacy of transperitoneal laparoscopic excision of primary seminal vesicle benign tumors (SVBTs) and summarize our experience with surgical techniques and follow-up outcomes of this rare condition. METHODS: This study included 6 patients who underwent transperitoneal laparoscopic excision of primary SVBTs between June 2005 and April 2011. A 5-port transperitoneal approach was used. The ipsilateral vas deferens was identified in the upper bulge of the retrovesical peritoneal reflection through a transverse approach and was dissected inwardly and used as a guide to the seminal vesicle tumor. Endoscopic Hem-o-lok clips (Teleflex Medical) were applied to control the vascular supply to the tumor base. With the contralateral vas deferens and seminal vesicle preserved, the tumor was removed together with the vas deferens and the adjoining ipsilateral seminal vesicle. The surgical procedures were successful in all 6 patients, without conversion to open surgery. The mean duration of surgery was 70 +/- 16 minutes (range, 50-100 minutes), with unremarkable blood loss of less than 50 mL. The mean postoperative hospital length of stay was 5.2 +/- 1.6 days (range, 4-8 days). No intra- or postoperative complications occurred. During a mean follow-up period of 42 +/- 24 months (range, 12-82 months), all patients remained asymptomatic, with preserved function as reported by the patient, and there was no evidence of recurrence. CONCLUSION: Our study demonstrated that transperitoneal laparoscopic excision of primary SVBTs is a viable option for minimally invasive treatment of SVBT.

[543]

TÍTULO / TITLE: - Expression of SOCSs in human prostate cancer and their association in prognosis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1007/s11010-013-1687-6
AUTORES / AUTHORS: - Zhu JG; Dai QS; Han ZD; He HC; Mo RJ; Chen G; Chen YF; Wu YD; Yang SB; Jiang FN; Chen WH; Sun ZL; Zhong WD
INSTITUCIÓN / INSTITUTION: - Department of Urology, Guizhou Provincial People’s Hospital, Guizhou, 550002, China.
RESUMEN / SUMMARY: - Suppressors of cytokine signaling (SOCS) proteins have been identified as negative feedback regulators of cytokine-mediated signaling in various tissues, and demonstrated to play critical roles in
tumorigenesis and tumor development of different cancers. The involvement of SOCSs in human prostate cancer (PCa) has not been fully elucidated. Thus, the aim of this study is to investigate the expression patterns and the clinical significance of SOCSs in PCa. The expression changes of SOCSs at mRNA and protein levels in human PCa tissues compared with adjacent benign prostate tissues were, respectively, detected by using real-time quantitative reverse transcriptase-polymerase chain reaction (QRT-PCR) and immunohistochemistry analyses. The associations of SOCSs expression with clinicopathological features and clinical outcome of PCa patients were further statistically analyzed. Among SOCSs, both QRT-PCR and immunohistochemistry analyses found that SOCS2 expression was upregulated (at mRNA level: change ratio = 1.98, P = 0.031; at protein level: 5.12 +/- 0.60 vs. 2.68 +/- 0.37, P = 0.016) and SOCS6 expression was downregulated (at mRNA level: change ratio = -1.65, P = 0.008; at protein level: 3.03 +/- 0.32 vs. 4.0.72 +/- 0.39, P = 0.004) in PCa tissues compared with those in non-cancerous prostate tissues. In addition, the upregulation of SOCS2 in PCa tissues was correlated with the lower Gleason score (P < 0.001), the absence of metastasis (P < 0.001) and the negative PSA failure (P = 0.009); the downregulation of SOCS6 tended to be found in PCa tissues with the higher Gleason score (P = 0.016), the advanced pathological stage (P = 0.007), the positive metastasis (P = 0.020), and the positive PSA failure (P = 0.032). Furthermore, both univariate and multivariate analyses showed that the downregulation of SOCS2 was an independent predictor of shorter biochemical recurrence-free survival. Our data offer the convincing evidence for the first time that the dysregulation of SOCS2 and SOCS6 may be associated with the aggressive progression of PCa. SOCS2 may be potential markers for prognosis in PCa patients.

[544]
TÍTULO / TITLE: - Short-term Functional Outcomes and Complications Associated With Transperineal Template Prostate Mapping Biopsy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Tsivian M; Abern MR; Qi P; Polascik TJ
INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Surgery, Duke University Medical Center, Durham, NC. Electronic address: matvey.tsivian@duke.edu.
RESUMEN / SUMMARY: - OBJECTIVE: To assess the complications and erectile and urinary functional outcomes of transperineal template mapping biopsy
(TTMB) of the prostate. METHODS: We retrospectively reviewed the records of 84 patients undergoing TTMB at our institution and recorded complications and functional outcomes. Erectile and urinary functions were measured at baseline, 2 weeks, and 6 +/- 2 weeks after TTMB using the International Index of Erectile Function short version (IIEF-5) and International Prostate Symptom Score questionnaires. Erectile and urinary function parameters were compared between baseline and 2 and 6 weeks after TTMB in a paired fashion. A subanalysis of erectile function was performed in preoperatively potent men (IIEF-5 >17). RESULTS: Sixteen patients (19%) experienced complications. The most common events were transient urinary retention (6%), prostatitis (4%) and local events, including perineal hematoma, bruising, or perineal pain (5%). One patient with hematuria required intervention. IIEF-5 scores at baseline, 2 weeks, and 6 weeks were 20 (interquartile range [IQR], 16-23), 18 (IQR, 12-22), and 18 (IQR, 12-22), respectively (P = .096 and P = .034). Among preoperatively potent men, IIEF-5 scores at baseline, 2 weeks, and 6 weeks were 22 (IQR, 20-24), 21 (IQR, 18-24), and 22 (IQR, 18-24), respectively (P = .011 and P = .018). International Prostate Symptom Scores were 6 (IQR, 3.5-11) at baseline, rose to 10 (IQR, 4.8-15) at 2 weeks (P = .012), and returned to 7 (IQR, 3.5-13) at 6 weeks (P = .628). CONCLUSION: TTMB has a favorable morbidity profile, with mostly mild and transient complications. Urinary retention occurred in 6%, and only 1 patient required intervention with bladder irrigation. Despite a statistically significant decline in erectile function from baseline, the median change in IIEF-5 score was 1 point. Urinary symptoms worsened initially but returned to baseline within 6 weeks.

[545]
TÍTULO / TITLE: - Sociodemographic disparities in the treatment of small renal masses.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Becker A; Roghmann F; Trinh QD; Hansen J; Tian Z; Shariat SF; Noldus J; Perrotte P; Graefen M; Karakiewicz PI; Sun M
INSTITUCIÓN / INSTITUTION: - Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Centre, Montreal, Canada; Martini-Clinic, Prostate Cancer Center Hamburg-Eppendorf, Hamburg, Germany.
RESUMEN / SUMMARY: - OBJECTIVE: To examine the presence of specific sociodemographic disparities in the treatment of individuals with small renal masses. PATIENTS AND METHODS: Patients diagnosed with pT1aNOM0 renal cell carcinoma (RCC) were identified from the Surveillance, Epidemiology, and End Results database (years 1988-2008). Treatment type was stratified into
non-surgical and surgical management and the group of patients who underwent surgical intervention was further stratified into those who underwent partial nephrectomy (PN) and those who underwent radical nephrectomy (RN). The main variables of interest were race and gender, as well as family income and poverty and education levels. Temporal trend analyses and logistic regression models were performed. RESULTS: Of 26,468 patients with T1aN0M0 RCC, 2,797 (10.6%) were non-surgically managed and 23,671 (89.4%) underwent surgery. Of the latter, 14,705 (62.1%) underwent RN and 8,966 (37.9%) PN. In multivariable analyses, black patients were 23% more likely to be non-surgically managed than other ethnic groups, and if surgically managed, were 20% less likely to undergo PN (both \( P \leq 0.007 \)). Men were 19% more likely than women to be non-surgically managed, but remained 14% more likely to receive a PN (both \( P < 0.001 \)). Treatment disparities according to income, education and poverty level were recorded. Poverty (odds ratio [OR]: 1.002) and education (OR: 0.998) proxies emerged as important determinants of non-surgical management, whereas income (OR: 1.08, all \( P \leq 0.02 \)) was a determinant of PN. CONCLUSIONS: Social inequalities regarding access to treatment remain prevalent among patients diagnosed with small renal masses. The persistence of such a phenomenon is a concerning trend which merits further investigation.
disorder, left-sided frontal headache and nausea; the patient had a previous history of metastatic prostate cancer. LM was diagnosed neuroradiologically with brain MRI and evidence of a detectable level of PSA in the cerebrospinal fluid. He was treated with docetaxel and prednisone for 3 cycles followed by external beam radiotherapy (EBRT) to the whole brain to a total dose of 30 Gy in 10 fractions with a simultaneous integrated boost to the macroscopic disease (total dose of 35 Gy in 10 fractions). No acute toxicity was observed.

RESULTS: A substantial clinical response was obtained after EBRT with neurological improvement and radiologically stable disease at post-treatment imaging until 10 weeks after radiation. The patient died of sudden general condition deterioration 3 months after EBRT. CONCLUSION: Since LM derived from prostate cancer is likely to become a more common clinical event, such patients would need to be included in clinical trials evaluating new therapeutic approaches, considering that the current treatment strategies have been shown to be rather ineffective.

[547]

TÍTULO / TITLE: - ERG Overexpression and PTEN Status Predict Capsular Penetration in Prostate Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Nagle RB; Algotar AM; Cortez CC; Smith K; Jones C; Sathyanarayana UG; Yun S; Riley J; Nagy D; Dittamore R; Dalkin B; Brosh L; Pestano G
INSTITUCIÓN / INSTITUTION: - Department of Pathology, University of Arizona, Tucson, Arizona; The University of Arizona Cancer Center, Tucson, Arizona.
RESUMEN / SUMMARY: - BACKGROUND: This study examines the combined effect of two common genetic alterations, ERG and PTEN, in prostate carcinoma progression. METHODS: Prostate tissue from 90 patients having unilateral capsular penetrating lesions, and a contra-lateral organ confined second lesion, were examined by immunohistochemistry for the expression of the TMPRSS2:ERG transformation product ERG and the loss of expression of PTEN, a powerful phosphatase inhibiting the PI3 kinase pathway. Multivariate logistic regression was carried out to analyze the data. RESULTS: After adjusting for Gleason score, the odds of having capsular penetration were 5.19 times higher (P = 0.015) for ERG+/PTEN- group as compared to the wild type (ERG-/PTEN+). CONCLUSIONS: This study presents the first evidence that ERG over expression and PTEN deletion is associated with greater risk of capsular penetration. Although further studies are needed, these results have the potential to change clinical assessment for prostate cancer. Prostate 9999:XX-XX. © 2013 Wiley Periodicals, Inc.

414
A New Proposed Rodent Model of Chemically Induced Prostate Carcinogenesis: Distinct Time-Course Prostate Cancer Progression in the Dorsolateral and Ventral Lobes.

TÍTULO / TITLE: - A New Proposed Rodent Model of Chemically Induced Prostate Carcinogenesis: Distinct Time-Course Prostate Cancer Progression in the Dorsolateral and Ventral Lobes.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Goncalves BF; de Campos SG; Zanetoni C; Scarano WR; Falleiros LR Jr; Amorim RL; Goes RM; Taboga SR

INSTITUCIÓN / INSTITUTION: - Department of Cell Biology, Institute of Biology, State University of Campinas (UNICAMP), Campinas, Brazil.

RESUMEN / SUMMARY: - BACKGROUND: Characterization of novel rodent models for prostate cancer studies requires evaluation of either spontaneous and carcinogen-induced tumors as well as tumor incidence in different prostatic lobes. We propose a new short-term rodent model of chemically induced prostate carcinogenesis in which prostate cancer progression occurs differentially in the dorsolateral and ventral lobes. METHODS: Adult gerbils were treated with MNU alone or associated with testosterone for 3 or 6 months of treatment. Tumor incidence, latency, localization, and immunohistochemistry (AR, PCNA, smooth muscle alpha-actin, p63, MGMT, and E-cadherin) were studied in both lobes. RESULTS: Comparisons between both lobes revealed that lesions developed first in the DL while the VL presented longer tumor latency. However, after 6 months, there was a dramatic increase in tumor multiplicity in the VL, mainly in MNU-treated groups. Lesions clearly progressed from a premalignant to a malignant phenotype over time and tumor latency was decreased by MNU + testosterone administration. Three-dimensional reconstruction of the prostatic complex showed that the DL developed tumors exclusively in the periurethral area and showed intense AR, PCNA, and MGMT immunostaining. Moreover, VL lesions emerged throughout the entire lobe. MNU-induced lesions presented markers indicative of an aggressive phenotype: lack of basal cells, rupture of the smooth muscle cell layer, loss of E-cadherin, and high MGMT staining. CONCLUSIONS: There are distinct pathways involved in tumor progression in gerbil prostate lobes. This animal provides a good model for prostate cancer since it allows the investigation of advanced steps of carcinogenesis with shorter latency periods in both lobes. Prostate © 2013 Wiley Periodicals, Inc.

Diffusion-weighted MR imaging of mucin-rich mucinous tubular and spindle cell carcinoma of the kidney: a case report.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.clinimag.2013.01.017
AUTORES / AUTHORS: - Tirumani SH; Assiri YI; Brimo F; Tsatoumas M; Reinhold C
INSTITUCIÓN / INSTITUTION: - Department of Imaging, Dana Farber Cancer Institute/Brigham and Women’s Hospital, Harvard Medical School, Boston, MA 02215. Electronic address: tirumani.sreeharsha@gmail.com.
RESUMEN / SUMMARY: - Mucinous tubular and spindle cell carcinoma (MTSCC) is a rare indolent subtype of renal cell carcinoma, which has variable magnetic resonance (MR) imaging features due to histomorphologic diversity. Diffusion-weighted MR imaging has shown its ability to differentiate benign and malignant renal neoplasms in some recent studies and can be a useful adjunct to routine MR sequences in ambiguous cases. We present a histopathology proven case of MTSCC highlighting the role of diffusion-weighted imaging in guiding the surgical management.

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[550]
TÍTULO / TITLE: - Re: barriers to the implementation of surveillance for stage I testicular seminoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.02.087
AUTORES / AUTHORS: - Richie JP

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[551]
- CASTELLANO -

TÍTULO / TITLE: Pharmaco-prevention et nutri-prevention des cancers de la prostate.
TÍTULO / TITLE: - Pharmaco and diet based prostate cancer prevention.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1684/bdc.2013.1739
AUTORES / AUTHORS: - Eisinger F; Cancel-Tassin G; Azzouzi AR; Gravis G; Rossi D; Cussenot O
INSTITUCIÓN / INSTITUTION: - Institut Paoli-Calmettes (IPC), departement d'anticipation et de suivi des cancers (Cancer Control Department), 232, boulevard Sainte-Marguerite, 13009 Marseille, France, Inserm, UMR 912,
In 2010, in France, 8,790 men died from prostate cancer despite a low and decreasing mortality rate. The individual risk/benefit ratio of prostate cancer screening is the focus of controversy and currently not in favor of a systematic screening program. Therefore, only prevention could reduce incidence, side effects of treatment and related mortality. Interestingly, prostate cancer prevention is also a field of controversy mainly about 5-alpha-reductase inhibitors. However, it could be expected that pharmaco- or diet-based prevention will be a huge tool for cancer control, even more for prostate cancer burden. This review comprehensively analyses which molecules or compounds could be used in preventive trials. With regard to pharmaco-prevention, three different kinds of drugs could be identified. First drugs, which aim at mainly or even solely reduce prostate cancer risk such as 5-alpha-reductase inhibitors and selective estrogen receptor modulators. Drugs, which aim at wider preventive impact such as: nonsteroidal anti-inflammatory drugs or difluoromethylornithine. Lastly, drugs for which reducing prostate cancer incidence is merely a side effect such as statins, metformin or histones desacetylase inhibitors. With regard to diet-based prevention, two main approaches could be identified: aliments and nutriments, on one hand, and vitamin and minerals, on the other. Interestingly if compounds reach experimental plausibility, natural foods or even global diet seem to have a higher impact. Lastly, besides assessment of efficacy, effectiveness required the critical step of compliance, which might actually be the weakest link of the prevention chain.
to 2010, 446 patients underwent nephroureterectomy for upper urinary tract cancer at our tertiary medical center. We included 115 patients who underwent preoperative diagnostic ureteroscopy and 281 patients who did not. This study analyzed the impact of the reported risk factors and diagnostic ureteroscopy for intravesical recurrence after nephroureterectomy by multivariate Cox regression model. RESULTS: The rates of metastasis and cancer-specific mortality did not differ significantly between the two groups. Diagnostic ureteroscopy was associated with a higher incidence of intravesical recurrence in patients with (p = 0.02) and without (p = 0.016) a previous history of bladder cancer. Ureter tumor biopsy (p = 0.272) and ureter involvement (p = 0.743) were not associated with the rate of intravesical recurrence in this study. Multivariate Cox regression analysis showed that only bladder cancer history (p < 0.001), multifocal tumor (p = 0.05), and diagnostic ureteroscopy (p = 0.05) were independently associated with intravesical recurrence. CONCLUSIONS: Diagnostic ureteroscopy for upper urinary tract cancer was not associated with metastasis and cancer-specific mortality. However, ureteroscopy was associated with an increased incidence of intravesical tumor recurrence. Methods of prevention should be considered to decrease intravesical recurrence and avoid repeated surgical interventions or the development of advanced bladder disease in patients at risk.

[553]

TÍTULO / TITLE: - Image visibility of cancer to enhance targeting precision and spatial mapping biopsy for focal therapy of prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ukimura O; de Castro Abreu AL; Gill IS; Shoji S; Hung AJ; Bahn D

INSTITUCIÓN / INSTITUTION: - Center of Image-Guided Surgery and Hillard and Roclyn Herzog Center for Robotic Surgery, USC Institute of Urology, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA.

RESUMEN / SUMMARY: - OBJECTIVE: To assess the advantages of cancer image visibility when using multiparametric transrectal ultrasonography (TRUS) in potential candidates for focal therapy for prostate cancer. PATIENTS AND METHODS: A total of 93 potential candidates for focal cryotherapy underwent grey-scale and Doppler TRUS-guided biopsy. All real-time TRUS images were recorded, allowing subsequent reviewing for the planning of targeted focal cryotherapy, and/or follow-up targeted biopsy. The spatial mapping of TRUS-visible lesions and targeted sampling areas were individually documented in schematic anatomic drawings of the prostate. Data from the baseline imaging-
targeted biopsies were compared with systematic (non-targeted) biopsies. Of the 93 patients, 73 patients with low- to intermediate-risk disease were eventually considered to be candidates for hemi-ablative focal cryosurgery, i.e. cryoablation of one lobe. RESULTS: Among the 93 patients, a total of 681 biopsy cores were available for analysis, including imaging-targeted (n = 256, 37.5%) and systematic (n = 425, 62.5%) cores. Of the 256 targeted biopsy cores, 65% (n = 167) were positive for cancer, compared with 6.2% (26/425) in systematic (non-targeted) cores (P < 0.001). A total of 88% (82/93) of the biopsy-proven cancer index lesions were TRUS-visible. When comparing TRUS-visible with image-invisible index lesions, the cancer-involved core length was 6.1 vs 1.5 mm (P < 0.001), respectively. Furthermore, the percent of core with involved cancer was 48 vs 16% (P < 0.001), and the mean Gleason score was 7.0 vs 6.2 (P < 0.001). With increasing TRUS-visible lesion size (<10, 11-15, 16-20, >20 mm), cancer-involved core length and percent of core with cancer also significantly increased (P = 0.009 and P = 0.008, respectively).

CONCLUSIONS: TRUS-guided targeted biopsies significantly improved the detection and staging of higher grade and larger volume cancer, compared with image-blind (non-targeted systematic) biopsies. Image visibility enhanced the precise targeting and accurate spatial mapping of cancer to help identify more appropriate candidates for focal therapy.

[554]

TÍTULO / TITLE: - Outcomes of Distal Ureteral Reconstruction Through Reimplantation With Psoas Hitch, Boari Flap, or Ureteroneocystostomy for Benign or Malignant Ureteral Obstruction or Injury.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Wenske S; Olsson CA; Benson MC

INSTITUCION / INSTITUTION: - Department of Urology, College of Physicians and Surgeons, Columbia University Medical Center, New York Presbyterian Hospital, New York, NY. Electronic address: sw2510@columbia.edu.

RESUMEN / SUMMARY: - OBJECTIVE: To assess functional outcomes and complications of ureteroneocystotomies (UNCs) with or without psoas hitch or Boari flap in the reconstruction and repair of the ureter. METHODS: We reviewed a consecutive series of patients that underwent open ureteral reconstruction for ureteral obstruction or injury. Underlying ureteral disorder, preoperative and postoperative estimated glomerular filtration rate (eGFR), and imaging studies regarding resolution of hydronephrosis were assessed. RESULTS: A total of 100 ureteral reimplantations performed at our institution
from November 1986 to August 2012 were identified: 24 primary ureteroneocystotomies, 58 with psoas hitch, and 18 with Boari flap. Median follow-up was 48.7 months (range 12.3-253 months). The most common underlying disorder was ureteral transitional cell cancer (TCC). Men were found to have more frequent underlying chronic ureteral disorders with chronic renal failure when compared to women. Ureteral stents were placed in 81% and were removed after a median of 33 days (range 2-161 days). Resolution of hydronephrosis was noted in 81% of the patients. The eGFR deteriorated significantly over time only in male patients (P = .001). Postoperative complications included stent-related dysuria, urinary tract infection, and contrast-extravasation on cystogram necessitating prolonged urethral and ureteral catheter drainage. CONCLUSION: Excellent functional outcome without significant morbidity associated with ureteral reimplantation/reconstruction was achieved. Despite resolution of hydronephrosis in the vast majority of patients, those with chronic underlying ureteral disorder and renal failure did not show improvement of their eGFR.

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TÍTULO / TITLE: - Re: explaining racial differences in prostate cancer mortality.  
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary  
AUTORES / AUTHORS: - Penson DF

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[556]

TÍTULO / TITLE: - Expanding utilization of robotic partial nephrectomy for clinical T1b and complex T1a renal masses.  
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary  
AUTORES / AUTHORS: - Borghesi M; Schiavina R; Gan M; Novara G; Mottrie A; Ficarra V  
INSTITUCIÓN / INSTITUTION: - OLV Robotic Surgery Institute, Moorselban 164, 9300, Aalst, Belgium, mark.borghesi@gmail.com.  
RESUMEN / SUMMARY: - INTRODUCTION: Partial nephrectomy is the standard of care for cT1a renal masses, offering equivalent oncologic outcomes and lower renal function impairment when compared to radical nephrectomy, with excellent overall survival results. Robot-assisted partial nephrectomy (RAPN)
allows to perform a precise tumor excision, simplifying the reconstruction steps of the procedure, especially in the treatment of complex or large renal tumors. Aim of this study was to summarize the available perioperative, functional, and oncological outcomes of RAPN performed for complex and/or large (cT1b) renal cell carcinoma (RCC). MATERIALS AND METHODS: We performed a nonsystematic review of the literature using a free-text protocol in the Medline database, using the terms “robot-assisted partial nephrectomy” and “robotic partial nephrectomy.” Two Authors reviewed separately to select RAPN series reporting data about complex and cT1b RCC. Other significant studies cited in the reference lists of the selected papers were also evaluated. EVIDENCE SYNTHESIS: According to the currently available evidences, RAPN offers promising results in terms of perioperative, functional, and oncological outcomes for the conservative management of complex or large renal tumors, even when compared with open and laparoscopic partial nephrectomy. Robot-assisted procedure allows surgeons to treat large and challenging renal masses, even if with higher warm ischemia time, operating time, and estimated blood loss in comparison with those obtained for the treatment of smaller lesions. CONCLUSIONS: In the hands of experienced surgeons, RAPN is a safe and reproducible approach for the treatment of cT1b and more challenging renal tumors, and could represent the way to expand the indications for minimally invasive conservative approach to RCC.

[557]  
**TÍTULO / TITLE:** - Microsatellite Instability and TARBP2 Mutation Study in Upper Urinary Tract Urothelial Carcinoma.  
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](1309/AJCPBSLP8XHSWLOW)  
**AUTORES / AUTHORS:** - Bai S; Nunez AL; Wei S; Ziober A; Yao Y; Tomaszewski JE; Bing Z  
**INSTITUCIÓN / INSTITUTION:** - Dept of Pathology, Sanford Clinic, 737 Broadway, Fargo, ND 58122; zhan-yong.bing@sanfordhealth.org.  
**RESUMEN / SUMMARY:** - Microsatellite instability (MSI) contributes to the tumorigenesis of upper urinary tract urothelial carcinomas (UUT-UCs). In this study, we first used MLH1 and MSH2 immunohistochemistry to identify patients with loss of expression of either or both of these proteins in 132 UUT-UCs. We found a total loss of MSH2 expression in 4 patients. MSI was evaluated using 5 markers in these 4 cases. All of the tumors had high MSI (MSI-H) status. Trans-activation responsive RNA-binding protein 2, an integral component of DICER1-containing complex, was a putative target of DNA mismatch repair deficiency.
Truncating mutation has been identified in gastrointestinal cancers with MSI. No previous study has evaluated the mutation status of this gene in MSI UUT-UCs. In this study, we analyze the mutation of TARBP2 in MSI-H UUT-UCs with reverse transcription polymerase chain reaction. No truncating mutations were identified in the MSI-H UUT-UCs.

[558]
**TÍTULO / TITLE:** Neoadjuvant carboplatin before radiotherapy in stage IIA and IIB seminoma.
**RESUMEN / SUMMARY:** [Enlace al Resumen / Link to its Summary](http://www.annonc/mdt148)
**REVISTA / JOURNAL:** Ann Oncol. 2013 Apr 16.
**AUTORES / AUTHORS:** Horwich A; Dearnaley DP; Sohaib A; Pennert K; Huddart RA
**INSTITUCIÓN / INSTITUTION:** Division of Radiotherapy & Imaging, The Institute of Cancer Research and Urological Oncology Unit.
**RESUMEN / SUMMARY:** BACKGROUND: Extended field radiotherapy is a standard of care for low volume stage II testicular seminoma. We hypothesized that neoadjuvant carboplatin might reduce the recurrence risk. PATIENTS AND METHODS: In a single-arm study, 51 patients were treated between May 1996 and November 2011 with a single cycle of carboplatin followed by radiotherapy. The radiation field was reduced from an extended abdomino-pelvic field to just the para-aortic region, and the radiation dose from 35 Gy to 30 Gy in 39 patients. RESULTS: After a median follow-up of 55 months (range 8-151 months) with 38 (74%) of the patients having been followed for >2 years, there have been no relapses (95% confidence limits of 5-year relapse-free survival of 93%-100%). Toxicity has been low with grade 3 toxicity limited to four patients with grade 3 haematological toxicity (with no clinical sequelae) and one patient with grade 3 nausea (during radiotherapy). No patients experienced grade 4 toxicity. CONCLUSIONS: The results of this pilot study suggest that a single cycle of neoadjuvant carboplatin before radiotherapy may reduce recurrence risk compared with radiotherapy alone and permit a smaller radiation field, and this approach is proposed for further investigation.

[559]
**TÍTULO / TITLE:** Oncogenic H-Ras reprograms Madin-Darby canine kidney (MDCK) cell-derived exosomal proteins following epithelial-mesenchymal transition.
**RESUMEN / SUMMARY:** [Enlace al Resumen / Link to its Summary](http://www.molcellproteomics.M112.027086)
**REVISTA / JOURNAL:** Mol Cell Proteomics. 2013 May 3.
**Enlace al texto completo (gratuito o de pago) 1074/mcp.M112.027086**
Epithelial-mesenchymal transition (EMT) is a highly conserved morphogenic process defined by the loss of epithelial characteristics and the acquisition of a mesenchymal phenotype. EMT is associated with increased aggressiveness, invasiveness, and metastatic potential in carcinoma cells. To assess the contribution of extracellular vesicles during EMT, we conducted a proteomic analysis of exosomes released from Madin Darby canine kidney (MDCK) cells, and MDCK cells transformed with oncogenic H-Ras (21D1 cells). Exosomes are 40 to 100 nm membranous vesicles originating from the inward budding of late endosomes and multivesicular bodies (MVBs) and are released from cells upon fusion of MVBs with the plasma membrane. Exosomes from MDCK cells (MDCK Exos) and 21D1 cells (21D1Exos) were purified from cell culture media using density gradient centrifugation (OptiPrep), and protein content identified by GeLC MS/MS proteomic profiling. Both MDCK- and 21D1-Exos populations were morphologically similar by cryoelectron microscopy and contained stereotypical exosomes marker proteins such as TSG101, Alix and CD63. In this study we show that the expression levels of typical EMT hallmark proteins seen in whole cells correlate with those observed in MDCKExos and 21D1Exos; i.e., reduction of characteristic inhibitor of angiogenesis, thrombospondin1 and epithelial markers Ecadherin, and EpCAM, with a concomitant up-regulation of mesenchymal makers such as vimentin. Further, we reveal that 21D1Exos are enriched with several proteases (e.g., MMP1, MMP14, MMP19, ADAM10, ADAMTS1), and integrins (e.g., ITGB1, ITGA3, ITGA6) that have been recently implicated in regulating the tumour microenvironment to promote metastatic progression. A salient finding of this study was the unique presence of key transcriptional regulators (e.g., the master transcriptional regulator YXB1) and core splicing complex components (e.g., SF3B1, SF3B3 and SFRS1) in mesenchymal 21D1Exos. Taken together, our findings reveal that exosomes from Ras-transformed MDCK cells are reprogrammed with factors which may be capable of inducing EMT in recipient cells.

[560]

**TITULO / TITLE:** - Clinical significance of protocadherin-8 (PCDH8) promoter methylation in bladder cancer.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](https://pubmed.ncbi.nlm.nih.gov/23339757/)

OBJECTIVE: To investigate the clinical significance of protocadherin-8 (PCDH8) promoter methylation in bladder cancer. METHODS: Methylation-specific polymerase chain reaction was used to examine the promoter methylation status of PCDH8 in tumour tissue samples obtained from patients with bladder cancer, and in normal bladder epithelial tissue samples obtained from age- and sex-matched control subjects. Methylation status was correlated with demographic, clinical and pathological parameters and disease outcome. RESULTS: PCDH8 promoter methylation was detected in 76/135 (56.3%) patients with bladder cancer and none of 34 (0%) control subjects. Methylation was significantly associated with advanced stage (T2-T4), high grade (G3), tumour recurrence, larger tumour diameter (>3 cm) and nonpapillary morphology. In addition, methylation was associated with significantly shorter survival time and was an independent predictor of overall survival. CONCLUSIONS: PCDH8 promoter methylation is a common occurrence in bladder cancer, and is associated with malignant behaviour and poor prognosis. Determination of PCDH8 promoter methylation status in tumour tissue may assist in the identification of patients who require aggressive postoperative intervention in order to improve prognosis.

TÍTULO / TITLE: - Target expression of Staphylococcus enterotoxin A from an oncolytic adenovirus suppresses mouse bladder tumor growth and recruits CD3+ T cell.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Han C; Hao L; Chen M; Hu J; Shi Z; Zhang Z; Dong B; Fu Y; Pei C; Wu Y

INSTITUCIÓN / INSTITUTION: - Department of Urology, The Affiliated School of Clinical Medicine of Xuzhou Medical College, Xuzhou Central Hospital, 199 Jie Fang Nan Road, Xuzhou, 221009, People’s Republic of China.

RESUMEN / SUMMARY: - We recently engineered an oncolytic adenovirus (PPE3-SEA) that expresses the superantigen, Staphylococcus enterotoxin A (SEA), and that has enhanced tumor specificity because the telomerase reverse transcriptase and hypoxia-inducible factor promoters regulate expression of E1A and E1B genes, respectively. Here, we evaluated the PPE3-SEA
adenovirus anti-tumor activity against MB49 mouse bladder cancer cell proliferation in vitro and in vivo. PPE3-SEA infection of murine MB49 cells in vitro induced cytopathic effects, and significant expression of SEA mRNA and protein, as measured by RT-PCR and western blot, respectively. Subcutaneous MB29 bladder tumors were established in syngeneic C57BL/6 mice. After 10 days, tumors were injected with either oncolytic virus or PBS. Tumor dimensions were measured on days 1, 3, 5, 7, 9, and 11 post-treatment and tumor volumes were calculated. One of eight PPE3-SEA-treated mice had no tumor by day 9. PPE3-SEA treated group had significantly lower mean tumor volume beginning on day 5 post-treatment (p < 0.01), more fibrous tissue in the tumor, and increased presence of infiltrating CD3+ T cells than those of the control group. Gross appearance and histologic sections from the livers and kidneys of the PPE3-SEA-treated group were similar to those of the control group. In conclusion, oncolytic adenoviruses can provide a novel delivery vehicle for SEA to tumor sites, and PPE3-SEA warrants further study as a potential anti-tumor agent for bladder cancer.

[562]
TÍTULO / TITLE: - Multiple squamous cell carcinomas following treatment with sorafenib for renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1111/j.1365-4632.2012.05485.x
AUTORES / AUTHORS: - El Tal AK; Remichofsky CJ; Mehregan DA; Ganger LK
INSTITUCIÓN / INSTITUTION: - Department of Dermatology, Wayne State University, Dearborn Georgetown Dermatologists, Sterling Heights Pinkus Dermatopathology Laboratory, Monroe, MI, USA.

[563]
TÍTULO / TITLE: - Prognostication of OCT4 isoform expression in prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1007/s13277-013-0817-9
AUTORES / AUTHORS: - de Resende MF; Chinen LT; Vieira S; Jampietro J; da Fonseca FP; Vassallo J; Campos LC; Guimaraes GC; Soares FA; Rocha RM
Cancer stem cells (CSCs) refer to a subset of tumor cells that self-renew and affect tumor heterogeneity. This model has attracted considerable interest in recent years due to its implications in the prognosis and clinical management of cancer because CSCs mediate the occurrence, growth, and recurrence of tumors. OCT4 is central to embryonic stem cell self-renewal and differentiation into specific lineages and encodes two chief isoforms that are generated by alternative splicing—OCT4A and OCT4B. Their function in prostate cancer (PCa) is unknown. The prognostic function of OCT4 isoforms in PCa samples was examined by immunohistochemistry (IHC) and sensitivity and specificity of the antibodies used were evaluated by molecular biology techniques. Biochemical and pathological data and specimens from 193 patients with PCa were evaluated retrospectively. IHC, western blot, immunofluorescence, and automated image analysis were also performed. IHC was performed on a tissue microarray, and western blot and immunofluorescence were performed using the PCa cell line DU-145. IHC expression of OCT4 isoforms correlated with biochemical and pathological parameters, particularly biochemical recurrence-free survival (BCRFS). Patients with higher levels of OCT4B had lower Gleason scores and decreased likelihood of experiencing biochemical recurrence (BR). OCT4A+ OCT4B-patients had the shortest BCRFS, and positivity for OCT4B expression was an independent prognostic factor for BCRFS in the multivariate analysis. We conclude that the expression of OCT4B is a strong marker of good prognosis, and its presence is associated with a decreased likelihood of BR. Thus, OCT4B might represent a powerful clinical prognostic biomarker for PCa patients.
Implantation in a prostate brachytherapy treatment procedure. Incorrect seed placement leads to both short and long term complications, including urethral and rectal toxicity. The authors present BrachyView, a novel concept of a fast intraoperative treatment planning system, to provide real-time seed placement information based on in-body gamma camera data. BrachyView combines the high spatial resolution of a pixellated silicon detector (Medipix2) with the volumetric information acquired by a transrectal ultrasound (TRUS). The two systems will be embedded in the same probe so as to provide anatomically correct seed positions for intraoperative planning and postimplant dosimetry. Dosimetric calculations are based on the TG-43 method using the real position of the seeds. The purpose of this paper is to demonstrate the feasibility of BrachyView using the Medipix2 pixel detector and a pinhole collimator to reconstruct the real-time 3D position of low dose-rate brachytherapy seeds in a phantom. METHODS: BrachyView incorporates three Medipix2 detectors coupled to a multipinhole collimator. Three-dimensionally triangulated seed positions from multiple planar images are used to determine the seed placement in a PMMA prostate phantom in real time. MATLAB codes were used to test the reconstruction method and to optimize the device geometry. RESULTS: The results presented in this paper show a 3D position reconstruction accuracy of the seed in the range of 0.5-3 mm for a 10-60 mm seed-to-detector distance interval (Z direction), respectively. The BrachyView system also demonstrates a spatial resolution of 0.25 mm in the XY plane for sources at 10 mm distance from Medipix2 detector plane, comparable to the theoretical value calculated for an equivalent gamma camera arrangement. The authors successfully demonstrated the capability of BrachyView for real-time imaging (using a 3 s data acquisition time) of different brachytherapy seed configurations (with an activity of 0.05 U) throughout a 60 x 60 x 60 mm(3) Perspex prostate phantom. CONCLUSIONS: The newly developed miniature gamma camera component of BrachyView, with its high spatial resolution and real time capability, allows accurate 3D localization of seeds in a prostate phantom. Combination of the gamma camera with TRUS in a single probe will complete the BrachyView system.

[565]
TITULO / TITLE: - Three-year Oncologic and Renal Functional Outcomes After Robot-assisted Partial Nephrectomy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.eururo.2013.03.052
RESUMEN / SUMMARY: - BACKGROUND: With the wider adoption of minimally invasive partial nephrectomy (PN), intermediate- and long-term outcomes data are needed to make firm conclusions about oncologic and functional efficacy, especially for robot-assisted PN (RPN). OBJECTIVE: To report intermediate-term oncologic and renal functional outcomes of RPN. DESIGN, SETTING, AND PARTICIPANTS: We performed a chart review of patients who had undergone RPN since June 2006; patients with a minimum of 2 yr of follow-up were included in this study. Length of follow-up was calculated from the date of surgery to the date of last clinical follow-up. Patients who were either lost to follow-up or who had follow-up outside of our center were sent surveys. INTERVENTION: Transperitoneal RPN with or without hilar clamping. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: The demographic, preoperative, and postoperative data were statistically analyzed. The Kaplan-Meier method was used to calculate overall survival (OS), cancer-specific survival (CSS), and cancer-free survival (CFS). Upstaging of chronic kidney disease (CKD) was calculated, as well. Univariate and multivariate analyses were performed to show predicting factors for the latest estimated glomerular filtration rate (eGFR). RESULTS AND LIMITATIONS: Of 427 patients, 134 had a minimum follow-up of 2 yr, and 70 had a minimum of 3-6 yr of follow-up. The mean age was 59.1 +/- 12.5 yr, body mass index (BMI) was 29.8 +/- 6.2 kg/m2, and Charlson comorbidity index (CCI) score was 4.2 +/- 1.6. The mean tumor size on computed tomography (CT) scan was 3.0 +/- 1.6 cm, RENAL score was 7.2 +/- 1.8, estimated blood loss (EBL) was 270.7 +/- 291.9 ml, operative time was 189.1 +/- 54.8 min, and warm ischemia time (WIT) was 17.9 +/- 10.3 min. A total of two intraoperative complications (1.5%) and five high-grade Clavien complications (3.7%) occurred. Patients stayed on average for 3.7 +/- 1.7 d in the hospital, and the average follow-up was 3.0 +/- 0.9 yr. OS was 97.01% at 3 yr and 90.20% at 5 yr; CFS was 98.92% at 3 yr and 98.92% at 5 yr; and CSS was 99.04%, as projected by the Kaplan-Meier method. The mean preoperative GFR was 88.2 +/- 0.8 ml/min per 1.73 m2; the latest postoperative GFR was 80 +/- 24 ml/min per 1.73 m2, with a 8 +/- 17.4% change. There was a 20.2% upstaging of CKD postoperatively, but no patients started dialysis. CONCLUSIONS: This study reaffirms that RPN is effective in renal function preservation and oncologic control at an intermediate follow-up interval.
TÍTULO / TITLE: - Prediction of rectum and bladder morbidity following radiotherapy of prostate cancer based on motion-inclusive dose distributions.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Thor M; Bentzen L; Hysing LB; Ekanger C; Helle SI; Karlsdottir A; Muren LP

INSTITUCIÓN / INSTITUTION: - Department of Medical Physics, Aarhus University Hospital, Aarhus, Denmark; Department of Oncology, Aarhus University Hospital, Aarhus, Denmark; Department of Clinical Medicine, Aarhus University, Aarhus, Denmark. Electronic address: mariator@rm.dk.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: In radiotherapy (RT) of prostate cancer the key organs at risk (ORs) - the rectum and the bladder - display considerable motion, which may influence the dose/volume parameters predicting for morbidity. In this study we compare motion-inclusive doses to planned doses for the rectum and bladder and explore their associations with prospectively recorded morbidity. MATERIALS AND METHODS: The study included 38 prostate cancer patients treated with hypo-fractionated image-guided intensity-modulated RT that had an average of nine repeat CT scans acquired during treatment. These scans were registered to the respective treatment planning CT (pCT) followed by a new dose calculation from which motion-inclusive dose distributions were derived. The pCT volumes, the treatment course averaged volumes as well as the planned and motion-inclusive doses were associated with acute and late morbidity (morbidity cut-off: Grade 2). RESULTS: Acute rectal morbidity (observed in 29% of cases) was significantly associated with both smaller treatment course averaged rectal volumes (population median: 75 vs. 94cm3) and the motion-inclusive volume receiving doses close to the prescription dose (2Gy-equivalent dose of 76Gy). CONCLUSION: Variation in rectum and bladder volumes leads to deviations between planned and delivered dose/volume parameters that should be accounted for to improve the ability to predict morbidity following RT.

[567]

TÍTULO / TITLE: - Ureteral stump carcinoma after trauma nephrectomy: a risk?

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Morris MW; Walker WB; Zhang X; Ahmed N; Vanderlan WB

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Mississippi School of Medicine, Jackson, Mississippi, USA.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.transproceed.2013.02.054
AUTORES / AUTHORS: - Tuzuner A; Cakir F; Akyol C; Celebi ZK; Ceylaner S; Ceylaner G; Sengul S; Keven K
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Ankara University Medical Faculty, Ankara, Turkey. Electronic address: atuzuner@yahoo.com.
RESUMEN / SUMMARY: - The risk of renal transplantation patients developing de novo malignancy is increased 100-fold compared with the healthy nontransplantation population. Renal cell carcinoma (RCC) arising from native kidneys is diagnosed among up to 4.6% of the renal transplant recipients as a consequence of immunosuppression. These tumors tend to behave more aggressively.(1) Although tumors occurring in allografted kidneys can be treated by partial (to save functional graft) or total nephrectomy, there is a paucity of data the outcomes. From 1978 to 2012, we performed 804 kidney transplantations including two cases in which RCC arose from the allografted kidney, both of which were treated with nephron-sparing surgery. The first patient has been followed for 30 months with a well functioning graft without an RCC recurrence. The second patient has returned to dialysis after 6 months due to an insufficient remnant nephron mass. In conclusion, nephron-sparing surgery is a novel alternative to total nephrectomy for allograft RCC. The remaining kidney can preserve function and the patient may not need chronic dialysis.

Circulating microRNAs as potential new biomarkers for prostate cancer.
TÍTULO / TITLE: - Circulating microRNAs as potential new biomarkers for prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.192
AUTORES / AUTHORS: - Sita-Lumsden A; Dart DA; Waxman J; Bevan CL
INSTITUCIÓN / INSTITUTION: - Androgen Signalling Laboratory, Department of Surgery and Cancer, Imperial College London, London W12 0NN, UK.
RESUMEN / SUMMARY: - Since they were first described in the 1990s, circulating microRNAs (miRNAs) have provided an active and rapidly evolving area of current research that has the potential to transform cancer diagnostics and therapeutics. In particular, miRNAs could provide potential new biomarkers for prostate cancer, the most common cause of cancer in UK men. Current diagnostic tests for prostate cancer have low specificity and poor sensitivity. Further, although many prostate cancers are so slow growing as not to pose a major risk to health, there is currently no test to distinguish between these and cancers that will become aggressive and life threatening. Circulating miRNAs are highly stable and are both detectable and quantifiable in a range of accessible bio fluids, thus have the potential to be useful diagnostic, prognostic and predictive biomarkers. This review aims to summarise the current understanding of circulating miRNAs in prostate cancer patients and their potential role as biomarkers.

[570]

TÍTULO / TITLE: - Dermo beta brachytherapy with 188-Re in squamous cell carcinoma of the penis: a new therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Carrozzo AM; Sedda AF; Muscardin L; Donati P; Cipriani C
INSTITUCIÓN / INSTITUTION: - Dermatology Department, Tor Vergata University, Rome, Italy.
RESUMEN / SUMMARY: - Background: Squamous cell carcinoma of the penis (SCCP) is the most common penis neoplasia, favoured by phimosis, HPV infection and scleroatrophic lichen. The classic therapy is surgical with anatomic demolition, which often causes important psychological problems. Other non-demolitive therapies can be utilized, such as radiotherapy, brachytherapy and topical medical treatment. Objectives: we propose a new non-invasive therapy called “Dermo beta brachytherapy (DBBT) with 188-Re” in which a synthetic inert resin-matrix containing a radioactive beta-emitting isotope is applied on the surface of the tumor lesion. Materials and methods: a total of 15 patients with a histologically confirmed diagnosis of SCCP were enrolled for treatment (DBBT). Results: of the 15 patients, 12 healed, 1 was lost at follow-up and 2 did not respond to therapy. Conclusion: The results indicate that DBBT is an effective treatment for SCC of the penis, sparing the anatomical integrity of the organ, and allowing normal sexual activity.
TÍTULO / TITLE: - Prostate-Specific Antigen Bounce After High-Dose-Rate Monotherapy for Prostate Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Mehta NH; Kamrava M; Wang PC; Steinberg M; Demanes J
INSTITUCIÓN / INSTITUTION: - University of California, Los Angeles, Los Angeles, California. Electronic address: nmehta@mednet.ucla.edu.
RESUMEN / SUMMARY: - PURPOSE: To characterize the magnitude and kinetics of prostate-specific antigen (PSA) bounces after high-dose-rate (HDR) monotherapy and determine relationships between certain clinical factors and PSA bounce. METHODS AND MATERIALS: Longitudinal PSA data and various clinical parameters were examined in 157 consecutive patients treated with HDR monotherapy between 1996 and 2005. We used the following definition for PSA bounce: rise in PSA >/=threshold, after which it returns to the prior level or lower. Prostate-specific antigen failure was defined per the Phoenix definition (nadir +2 ng/mL). RESULTS: A PSA bounce was noted in 67 patients (43%). The number of bounces per patient was 1 in 45 cases (67%), 2 in 19 (28%), 3 in 2 (3%), 4 in 0, and 5 in 1 (1%). The median time to maximum PSA bounce was 1.3 years, its median magnitude was 0.7, and its median duration was 0.75 years. Three patients (2%) were noted to have PSA failure. None of the 3 patients who experienced biochemical failure exhibited PSA bounce. In the fully adjusted model for predicting each bounce, patients aged <55 years had a statistically significant higher likelihood of experiencing a bounce (odds ratio 2.22, 95% confidence interval 1.38-3.57, P=.001). There was also a statistically significant higher probability of experiencing a bounce for every unit decrease in Gleason score (odds ratio 1.52, 95% confidence interval 1.01-2.04, P=.045).
CONCLUSIONS: A PSA bounce occurs in a significant percentage of patients treated with HDR monotherapy, with magnitudes varying from <1 in 28% of cases to >/=1 in 15%. The median duration of bounce is <1 year. More bounces were identified in patients with lower Gleason score and age <55 years. Further investigation using a model to correlate magnitude and frequency of bounces with clinical variables are under way.

TÍTULO / TITLE: - Potential relationship between BK virus and renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
The objective of the present study was to investigate the potential association between the presence of BK virus (BKV) DNA and mRNA and renal cell carcinoma and bladder transitional cell carcinoma. The formalin-fixed and paraffin-embedded tissue samples were obtained from 50 cancer patients with renal cell carcinoma, 40 cancer patients with bladder transitional cell carcinoma, 45 control patients with the benign renal pathology, and from another 25 control patients with benign bladder pathology. The samples were subjected to nested PCR for detection of BKV DNA and real-time reverse transcription PCR (real-time RT-PCR) for determining mRNA levels of BKV. The results of the nested PCR indicated that 23 (14.3%) of 160 samples were positive for BKV DNA. The relationship between the cancer and the presence of BKV DNA was significant (P < 0.05). The BKV DNA positivity was significantly associated with the histological diagnosis of renal cell carcinoma (P = 0.03), but not with that of bladder transitional cell carcinoma. The results of real-time RT-PCR showed that the mRNA of BKV VP1 was present in 69.5% of the BKV DNA positive samples. The levels of BKV mRNA were significantly higher in the renal cell cancer samples than in the control samples (P < 0.05). The results of the present study confirm the association between BKV and renal cell cancer. The findings also indicated that the presence of BKV DNA resulted in a fivefold increase in the risk of development of renal cell carcinoma.
OBJECTIVE: To investigate the expression pattern of Sprouty2 (Spry2) and its clinicopathologic significance among patients with renal cell carcinoma (RCC) and to detect its role in proliferation and invasion of RCC in vitro. MATERIALS AND METHODS: The expression profile of Spry2 in RCC and matched adjacent noncancerous tissues were detected by immunohistochemistry and Western blot analysis. The expression of Spry2 was depleted by stably transfecting with small, interfering ribonucleic acid and the effects of Spry2 were assessed using the cell proliferation and transwell assay. RESULTS: We found Spry2 protein expressed at lower levels and modestly downregulated in cancerous RCC tissues compared with adjacent normal tissue (P <.001). We also measured the expression level of Spry2 in 103 archived RCC tissues by immunohistochemical staining and found its correlation with clinicopathologic findings such as tumor size (P = .002), pathologic TNM stage (P <.001), tumor grade (P <.001), lymph node metastasis (P = .001), distant metastasis (P <.001), and poor survival (P = .001). In addition, small interfering ribonucleic acid-induced depletion of Spry2 expression promoted proliferation and invasion in RCC cell lines. CONCLUSION: Collectively, our results have demonstrated for the first time, to our knowledge, that Spry2 might offer an attractive new target for prognostic and therapeutic intervention in RCC.
pulses of intensity 200kV/m; however, with 400 pulses we observed the
degeneration and shrinkage of testicular tissues along with a significant
increase in apoptotic rate. Moreover, in the 100- and 200-EMP groups, a non-
significant increase in TGF-beta3 mRNA and protein expression was observed,
whereas in the 400-EMP group a significant increase was observed (P<0.05).
These results indicate that increase in the apoptotic rate of testicular tissues
and increase in TGF-beta3 expression may be one of the mechanisms for EMP-
induced increase in BTB permeability in mice.

[575]
TÍTULO / TITLE: - Is Fluorescent Fystoscopy of Cost/Benefit/Therapeutic Value for Carcinoma In Situ of the Bladder? No (a difficult task).
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.04.039
AUTORES / AUTHORS: - O’Brien T
INSTITUCIÓN / INSTITUTION: - Urology Centre, Guys and St. Thomas Hospitals, London, UK.

[576]
TÍTULO / TITLE: - Is Fluorescent Cystoscopy of Cost/Benefit/Therapeutic Value for Carcinoma In Situ of the Bladder? Yes.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.04.038
AUTORES / AUTHORS: - Witjes JA
INSTITUCIÓN / INSTITUTION: - Department of Urology, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.

[577]
TÍTULO / TITLE: - 125I brachytherapy for localized prostate cancer: a single institution experience.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1700/1248.13793
AUTORES / AUTHORS: - Guarneri A; Botticella A; Filippi AR; Munoz F; Beltramo G; Casetta G; Giglioli FR; Tizzani A; Ragona R; Ricardi U
AIMS AND BACKGROUND: To evaluate the clinical outcome of a cohort of localized prostate cancer patients treated with 125I permanent brachytherapy at the University of Turin. METHODS AND STUDY DESIGN: A retrospective analysis was carried out on 167 consecutive patients with early stage prostate adenocarcinoma who underwent 125I brachytherapy between January 2003 and December 2010. A minimum follow-up of \( \geq 12 \) months was mandatory for inclusion. Biochemical disease-free survival (defined on the basis of the ASTRO definition and the ASTRO-Phoenix definition) was chosen as the primary end point. Secondary end points were gastrointestinal and genitourinary toxicity (acute and late, defined according to the RTOG scale).

RESULTS: With a median follow-up of 42 months (range, 13.5-90.7), biochemical disease-free survival at 3 and 5 years was respectively 91.1\% and 85.7\%, according to the ASTRO definition and 94.5\% and 85.1\% according to ASTRO-Phoenix definition (for statistical purposes, only the ASTRO definition was used). Hormone treatment and nadir PSA (cutoff of 0.35 ng/ml) were the only factors affecting biochemical disease-free survival both on univariate (P = 0.02 and P = 0.001, respectively) and multivariate analysis (HR 0.024; P = 0.021 and HR 21.6; P = 0.006, respectively). Only 3.6\% of patients experienced \( \geq \) grade 3 acute urinary toxicity and 5\% \( \geq \) grade 3 late urinary toxicity. Prior transurethral prostate resection was the only independent predictor of grade 3 late urinary toxicity on multivariate analysis (HR 0.13; P = 0.009).

CONCLUSIONS: This mono-institutional series confirmed that brachytherapy is an effective and safe treatment modality for localized prostate cancer, with acceptable short- and long-term morbidity rates.

[578]

**TITULO / TITLE:** - Diagnosis of relevant prostate cancer using supplementary cores from magnetic resonance imaging-prompted areas following multiple failed biopsies.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


   ●●Enlace al texto completo (gratuito o de pago) 1016/j.mri.2013.02.007

**AUTORES / AUTHORS:** - Costa DN; Bloch BN; Yao DF; Sanda MG; Ngo L; Genega EM; Pedrosa I; Dewolf WC; Rofsky NM

**INSTITUCIÓN / INSTITUTION:** - Department of Radiology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA; Department of Radiology, UT Southwestern Medical Center, Dallas, TX, USA. Electronic address: daniel.costa@utsouthwestern.edu.
RESUMEN / SUMMARY: - OBJECTIVES: To establish the value of MRI in targeting re-biopsy for undiagnosed prostate cancer despite multiple negative biopsies and determine clinical relevance of detected tumors. MATERIALS AND METHODS: Thirty-eight patients who underwent MRI after 2 or more negative biopsies due to continued clinical suspicion and later underwent TRUS-guided biopsy supplemented by biopsy of suspicious areas depicted by MRI were identified. Diagnostic performance of endorectal 3T MRI in diagnosing missed cancer foci was assessed using biopsy results as the standard of reference. Ratio of positive biopsies using systematic versus MRI-prompted approaches was compared. Gleason scores of detected cancers were used as surrogate for clinical relevance. RESULTS: Thirty-four percent of patients who underwent MRI before re-biopsy had prostate cancer on subsequent biopsy. The positive biopsy yield with systematic sampling was 23% versus 92% with MRI-prompted biopsies (p<0.0001). Seventy-seven percent of tumors were detected exclusively in the MRI-prompted zones. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI to provide a positive biopsy were 92%, 60%, 55%, 94% and 71%, respectively. The anterior gland and apical regions contained most tumors; 75% of cancers detected by MRI-prompted biopsy had Gleason score >/= 7. CONCLUSIONS: Clinically relevant tumors missed by multiple TRUS-guided biopsies can be detected by a MRI-prompted approach.

[579]
TÍTULO / TITLE: - Re: protease nexin 1 inhibits hedgehog signaling in prostate adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.02.105
AUTORES / AUTHORS: - Atala A

[580]
TÍTULO / TITLE: - Large-scale independent validation of the nuclear factor-kappa B p65 prognostic biomarker in prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.ejca.2013.02.026
AUTORES / AUTHORS: - Gannon PO; Lessard L; Stevens LM; Forest V; Begin LR; Minner S; Tennstedt P; Schlomm T; Mes-Masson AM; Saad F
INSTITUCIÓN / INSTITUTION: - Centre de recherche du Centre hospitalier de l'Université de Montreal (CRCHUM), Institut du cancer de Montreal, and Faculty of Medicine, Université de Montreal, Montreal, Quebec, Canada.

RESUMEN / SUMMARY: - PURPOSE: Over the last decade, we and others have uncovered a robust association between the nuclear localisation of nuclear factor-kappa B (NF-kappaB) p65, prostate cancer (PCa) aggressiveness and biochemical recurrence (BCR). Our goal was to validate these results in a large independent cohort of PCa patients who underwent radical prostatectomy.

EXPERIMENTAL DESIGN: A set of 1826 fully annotated prostate cancers treated by radical prostatectomy were analysed in a tissue microarray (TMA) format for NF-kappaB p65 immunohistochemistry-based protein expression. We performed standard Cox proportional hazard regression models for follow-up data, bootstrap procedure for model internal validation, Harrell’s concordance index for model discrimination and graphical assessment of predicted versus actual outcomes for model calibration.

RESULTS: We observed a significant association between an increase in the nuclear frequency of NF-kappaB p65 and Gleason score (P<0.001), overall BCR (P<0.001) and development of metastases (P=0.001). NF-kappaB was found to be an independent predictor of BCR (P<0.001, Cox regression). However its contribution to the predictive accuracy of a multivariate model, which included preoperative PSA, Gleason score, extraprostatic extension, lymph node invasion, seminal vesicle involvement and surgical margin status, was modest. CONCLUSIONS: Our study offers validating results linking NF-kappaB p65 with disease progression using a large cohort of European men. However, the contribution of NF-kappaB to a post-surgical predictive model appears modest. Further validating work should focus on evaluating the contribution of NF-kappaB p65 in pre-treatment models.

[581]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hoeks CM; Vos EK; Bomers JG; Barentsz JO; Hulsbergen-van de Kaa CA; Scheenen TW

INSTITUCIÓN / INSTITUTION: - From the *Departments of Radiology, and daggerPathology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.
RESUMEN / SUMMARY: - OBJECTIVES: The objective of this study was to evaluate the apparent diffusion coefficient (ADC) of diffusion-weighted magnetic resonance (MR) imaging for the differentiation of transition zone cancer from non-cancerous transition zone with and without prostatitis and for the differentiation of transition zone cancer Gleason grade (GG) using MR-guided biopsy specimens as a reference standard. MATERIALS AND METHODS: From consecutive MR-guided prostate biopsies (2008-2012) in our referral center, we retrospectively included patients from whom diffusion-weighted MR imaging ADC values were acquired during MR-guided biopsy and whose biopsy cores had a (cancer) core length 10 mm or greater and originated from the transition zone. Two radiologists, who were blinded to the ADC data, annotated regions of interest on biopsy sampling locations of MR-guided biopsy confirmation scans in consensus. Median ADC (mADC) of the regions of interest was related to histopathology outcome in MR-guided biopsy core specimens. Mixed model analysis was used to evaluate mADC differences between 7 histopathology categories predefined as MR-guided biopsy core specimens with primary and secondary GG 4-5 (I), primary GG 4-5 secondary GG 2-3 (II), primary GG 2-3 secondary GG 4-5 (III) and primary and secondary GG 2-3 cancer (IV), and noncancerous tissue without (V) or with degree 1 (VI) or degree 2 prostatitis (VII). Diagnostic accuracy was evaluated using areas under the receiver operating characteristic (AUC) curve. RESULTS: Fifty-two patients with 87 cancer-containing biopsy cores and 53 patients with 101 non-cancerous biopsy cores were included. Significant mean mADC differences were present between cancers (mean mADC, 0.77-0.86 x 10 mm/s) and noncancerous transition zone without (1.12 x 10 mm/s) and with degree 1 to 2 prostatitis (1.05-1.12 x 10 mm/s; P < 0.0001-0.05). Exceptions were mixed primary and secondary GG cancers versus a degree 2 of prostatitis (P = 0.06-0.09). No significant differences were found between subcategories of primary and secondary GG cancers (P = 0.17-0.91) and between a degree 1 and 2 prostatitis and non-cancerous transition zone without prostatitis (P = 0.48-0.94). The mADC had an AUC of 0.84 to differentiate cancer versus non-cancerous transition zone. AUCs of 0.84 and 0.56 were found for mADC to differentiate prostatitis from cancer and from non-cancerous transition zone. The mADC had an AUC of 0.62 to differentiate a primary GG 4 versus GG 3 cancer. CONCLUSIONS: The mADC values can differentiate transition zone cancer from non-cancerous transition zone and from a degree 1, and from most cases of a degree 2 prostatitis. However, because of substantial overlap, mADC has a moderate accuracy to differentiate between different primary and secondary GG subcategories and cannot be used to differentiate non-cancerous transition zone from degrees 1 to 2 of prostatitis. Diffusion-weighted imaging ADC may therefore contribute in the detection of transition zone cancers; however, as a single functional MR imaging technique, diffusion-weighted imaging has a moderate diagnostic accuracy in separating higher from
lower GG transition zone cancers and in differentiating prostatitis from non-cancerous transition zone.

[582]
TÍTULO / TITLE: - Role of high-field MR in studies of localized prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Lagemaat MW; Scheenen TW
INSTITUCIÓN / INSTITUTION: - Department of Radiology (766), Radboud University Nijmegen Medical Centre, The Netherlands.
RESUMEN / SUMMARY: - Magnetic resonance imaging is attracting increasing attention from the uroradiological community as a modality to guide the management of prostate cancer. With the high incidence of prostate cancer it might come as a surprise that for a very long time (and in many places even at present) treatment decisions were being made without the use of detailed anatomical and functional imaging of the prostate gland at hand. Although T2-weighted MRI can provide great anatomical detail, by itself it is not specific enough to discriminate cancer from benign disease, so other functional MRI techniques have been explored to aid in detection, localization, staging and risk assessment of prostate cancer. With the current evolution of clinical MR systems from 1.5 to 3 T it is important to understand the advantages and the challenges of the higher magnetic field strength for the different functional MR techniques most used in the prostate: T2-weighted MRI, diffusion-weighted MRI, MR spectroscopic imaging and dynamic contrast-enhanced imaging. In addition to this, the use of the endorectal coil at different field strengths is discussed in this review, together with an outlook of the possibilities of ultra-high-field MR for the prostate. Copyright © 2013 John Wiley & Sons, Ltd.

[583]
TÍTULO / TITLE: - Diffusion-weighted MRI and its role in prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Tamada T; Sone T; Jo Y; Yamamoto A; Ito K
INSTITUCIÓN / INSTITUTION: - Department of Radiology, Kawasaki Medical School, Kurashiki City, Okayama, Japan.
RESUMEN / SUMMARY: - In the last 5 years, the multiparametric approach has been investigated as the method for the MRI of prostate cancer. In multiparametric MRI of the prostate, at least two functional MRI techniques, such as diffusion-weighted MRI (DW-MRI) and dynamic contrast-enhanced
MRI, are combined with conventional MRI, such as T2-weighted imaging. DW-MRI has the ability to qualitatively and quantitatively represent the diffusion of water molecules by the apparent diffusion coefficient, which indirectly reflects tissue cellularity. DW-MRI is characterized by a short acquisition time without the administration of contrast medium. Thus, DW-MRI has the potential to become established as a noninvasive diagnostic method for tumor detection and localization, tumor aggressiveness, local staging and local recurrence after various therapies. Accordingly, radiologists should recognize the principles of DW-MRI, the methods of image acquisition and the pitfalls of image interpretation. Copyright © 2013 John Wiley & Sons, Ltd.

[584]
TÍTULO / TITLE: - Re: relationship of sex hormones and nocturia in lower urinary tract symptoms induced by benign prostatic hyperplasia.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kaplan SA

[585]
TÍTULO / TITLE: - Transrectal electrical impedance tomography of the prostate: Spatially coregistered pathological findings for prostate cancer detection.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wan Y; Borsic A; Heaney J; Seigne J; Schned A; Baker M; Wason S; Hartov A; Halter R
INSTITUCIÓN / INSTITUTION: - Thayer School of Engineering at Dartmouth, 14 Engineering Drive, Hanover, New Hampshire 03755.
RESUMEN / SUMMARY: - Purpose: Prostate cancer ranks as one of the most common malignancies and currently represents the second leading cancer-specific cause of death in men. The current use of single modality transrectal ultrasound (TRUS) for biopsy guidance has a limited sensitivity and specificity for accurately identifying cancerous lesions within the prostate. This study introduces a novel prostate cancer imaging method that combines TRUS with electrical impedance tomography (EIT) and reports on initial clinical findings based on in vivo measurements.Methods: The ultrasound system provides anatomic information, which guides EIT image reconstruction. EIT reconstructions are correlated with semiquantitative pathological findings. Thin
Plate spline warping transformations are employed to overlay electrical impedance images and pathological maps describing the spatial distribution of prostate cancer, with the latter used as reference for data analysis. Clinical data were recorded from a total of 50 men prior to them undergoing radical prostatectomy for prostate cancer treatment. Student’s t-tests were employed to statistically examine the electrical property difference between cancerous tissue and benign tissue as defined through histological assessment of the excised gland. Results: Example EIT reconstructions are presented along with a statistical analysis comparing EIT and pathology. An average transformation error of 1.67% is found when 381 spatially coregistered pathological images are compared with their target EIT reconstructed counterparts. At EIT signal frequencies of 0.4, 3.2, and 25.6 kHz, paired-testing demonstrated that the conductivity of cancerous regions is significantly greater than that of benign regions (p < 0.0304). Conclusions: These preliminary clinical findings suggest the potential benefits electrical impedance measurements might have for prostate cancer detection.

[586]

TITULO / TITLE: Id-like reaction to BCG therapy for bladder cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Lowther C; Miedler JD; Cockerell CJ
INSTITUCIÓN / INSTITUTION: Big Horn Basin Skin Center, Cody, Wyoming, USA.
RESUMEN / SUMMARY: Id reaction, also known as autoeczematization, is the development of dermatitis that is distant to an initial site of infection or sensitization. Clinical findings typically include an acute, intensely pruritic maculopapular or papulovesicular eruption that most frequently involves the extremities. Histology typically reveals spongiotic dermatitis that often is vesicular, and eosinophils may be present in the infiltrate. Id reactions can result from inflammatory skin conditions such as stasis dermatitis as well as infectious entities including mycobacterial infections. BCG live therapy consists of an attenuated strain of Mycobacterium bovis that is utilized as a first-line treatment of superficial transitional cell carcinomas. We report the case of an id-like reaction in a 90-year-old man who developed an intensely pruritic, scaly, erythematous eruption on all 4 extremities 2 weeks after starting weekly intravesical use of BCG therapy for superficial transitional cell carcinoma. A representative biopsy demonstrated spongiotic dermatitis with overlying scaling and an eosinophilic infiltrate. The eruption resolved after discontinuation of BCG therapy and treatment with topical corticosteroids.

[587]
**TÍTULO / TITLE:** The Impact Of Histologic Reclassification During Pathology Re-Review: Evidence Of A Will Rogers Effect In Bladder Cancer?

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Linder BJ; Boorjian SA; Cheville JC; Sukov WR; Thapa P; Tarrell RF; Frank I

**INSTITUCIÓN / INSTITUTION:** Department of Urology, Mayo Clinic, Rochester, MN.

**RESUMEN / SUMMARY:** PURPOSE: To investigate the association of histologic reclassification during pathology re-review of RC specimens with clinicopathologic outcomes among patients initially classified as having UC. MATERIALS AND METHODS: We identified 1,211 patients initially diagnosed with UC at RC between 1980-2005. All pathologic specimens were re-reviewed by a urologic pathologist. Survival was estimated using Kaplan-Meier method and compared with the log-rank test. RESULTS: A total of 406/1,211 (33%) cases previously recorded as pure UC were re-classified with variant histology. The most common variant histologies identified were squamous (n=151;37%) and micropapillary (n=62;15%). Variant histology on re-review was associated with a higher rate of extravesical disease (71%) than UC at initial diagnosis (52%) or pure UC on re-review (42%;p<0.0001). Median postoperative follow-up was 11.1 years, during which 976 patients died, including 564 dying of bladder cancer. Notably, reclassification resulted in significant stratification of 10-year cancer-specific survival (CSS), which was 50% for patients with pure UC after re-review, 47% among patients with UC on initial interpretation, and 42% for patients with variant histology on re-review (p=0.03). Likewise, 10-year overall survival among patients with UC on re-review, UC at initial interpretation, and variant histology on re-review were 29%, 27%, and 24%, respectively (p=0.04). CONCLUSIONS: Pathologic re-review of RC specimens identified variant histology in one-third of patients. These variants are associated with a high rate of locally-advanced disease, which may impact the noted rates of CSS and OS. Thus, re-review status is critical to be aware of when interpreting outcomes from historical datasets and performing risk stratification.

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[588]

**TÍTULO / TITLE:** Perioperative chemotherapy: when to use it, what to use, and why.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**Enlace al texto completo (gratis o de pago) 1016/j.ucl.2013.01.001**
RESUMEN / SUMMARY: This article provides an overview of intravesical chemotherapy agents used for non-muscle invasive bladder cancer; summarizes the evidence on single-dose perioperative administration, induction therapy, and maintenance therapy; and briefly discusses ongoing research.

TÍTULO / TITLE: Lipids, LXRs and prostate cancer: Are HDACs a new link?
RESUMEN / SUMMARY: Lipids play a complex role in prostate cancer (PCa). Increased de novo synthesis of fatty acids and/or cholesterol is associated with the development of prostate tumors. Liver X Receptors (LXRs) are members of the nuclear receptor family that regulates intracellular lipid homeostasis. Targeting the transcriptional activity of LXRs has, therefore, been proposed as a mechanism for attenuating the progression of PCa. Histone Deacetylases (HDACs), however, have a negative effect on LXR activity. Therefore, HDAC inhibition reduces intracellular cholesterol levels and thereby decreases tumor cell proliferation. LXRs and HDAC inhibitors can, therefore, inhibit tumor proliferation. This review discusses the interacting roles of lipids, LXRs and HDACs in the development of PCa, where increased lipid levels enhance HDAC activity thereby altering LXR-dependent regulation of cellular lipid homeostasis. It provides a new paradigm for the treatment of prostate cancer, where LXRs are activated and HDACs repressed.

TÍTULO / TITLE: Estudio comparativo de morbimortalidad entre conducto ileal y ureterosigmoidostomía tras cistectomía radical por neoplasia vesical.
Comparative Study of Morbidity and Mortality Between Ileal Conduit and Ureterosigmoidostomy After Radical Cystectomy for Bladder Neoplasm.

OBJECTIVES: Despite the growing trend in the development of orthotopic neobladders, the procedure cannot be performed in many cases, thereby retaining the validity of other techniques. We propose a comparative analysis between patients with radical cystectomy for bladder neoplasm and reconstruction using the ileal conduit (IC) or ureterosigmoidostomy (USG). PATIENTS AND METHOD: Observational retrospective study on 255 patients with radical cystectomy between 1985 and 2009, selecting group assignments by the use of IC and USG. Analysis of the demographic and preoperative characteristics, perioperative complications, pathology and medium to long-term complications. Comparison of groups using T-Student, U-Mann-Whitney and chi square tests, with P<.05 indicating statistical significance. Preparation of survival tables according to Kaplan-Meier, establishing comparisons using the log-rank test. RESULTS: There were 41 cases of IC and 55 cases of USG, with a mean patient age of approximately 61 years. USGs were performed on a greater number of females than ICs. There were no differences in the need for transfusion, with similar results as other series. There was a greater trend towards the appearance of intestinal fistulae and greater morbidity and mortality in the postoperative period in USG, although it was not significant. There was a greater long-term presence of eventrations in IC, and of pyelonephritis and the need for taking alkalinizing agents in USG. The appearance of peristomal hernias in IC was less than in previous series. With a mean follow-up greater than 50 months, the overall survival was 40% at 5 years, with no differences according to urinary diversion. CONCLUSIONS: IC and USG are two applicable urinary diversions in the event that orthotopic neobladder surgery cannot be performed. They have a similar long-term complication and survival profile in our series, although with a higher morbidity in postoperative complications for USG.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Wood DP

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TÍTULO / TITLE: - Three-dimensional summation of rectal doses in brachytherapy combined with external beam radiotherapy for prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Kikuchi K; Nakamura R; Tanji S; Yamaguchi S; Kakuahara H; Yabuuchi T; Inatsu W; Oikawa H; Ariga H

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Iwate Medical University School of Medicine. Electronic address: kikuchi@iwate-med.ac.jp.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: To determine the dose constraints for rectal bleeding in brachytherapy (BRT) combined with external beam radiotherapy (EBRT). MATERIALS AND METHODS: Post-BRT, pelvic computed tomography images were used for subsequent EBRT planning and BRT postplans in 37 patients. The physical doses for each plan were converted to biologically effective doses, and corresponding voxel doses were integrated to plot the summed dose-volume histogram (sum-DVH). Between 5 patients with (bled-pts) and 32 without (spared-pts) grade 2 or 3 rectal bleeding, the differences in the mean minimal dose (rDn) covering the rectal volume of 0.5-10.0cc and the rectal volume (rVn) receiving the calculated dose of 20-150Gy were compared. RESULTS: The differences in the summed-rDn were determined by BRT exposure, while those of the summed-rVn were determined in the low-dose range and superimposed in the high-dose range by EBRT exposure. Of the 13 patients with rV150 of >1.2cc, 4 were bled-pts (30.8%). Of the 24 patients with rV150 of <=1.2cc, 1 was a bled-pts (4.2%) (p=0.024; odds ratio, 10.2; CI (95%), 1.0-104.3). CONCLUSIONS: The mono-scale DVH analysis is a promising method for exploring the threshold for rectal bleeding in combined radiotherapy.

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[592]

[593]
TÍTULO / TITLE: Gleason 6 Prostate Tumors Diagnosed in the PSA Era Do Not Demonstrate the Capacity for Metastatic Spread at the Time of Radical Prostatectomy.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Donin NM; Laze J; Zhou M; Ren Q; Lepor H

INSTITUCIÓN / INSTITUTION: Department of Urology, New York University School of Medicine, New York, NY. Electronic address: Nicholas.Donin@nyumc.org.

RESUMEN / SUMMARY: OBJECTIVE: To elucidate the probability that Gleason 6 tumors diagnosed in the prostate-specific antigen (PSA) era treated with radical prostatectomy (RP) develop metastasis. METHODS: Between October 2000 and June 2012, 1781 men underwent open RP by a single surgeon. Biochemical recurrence (BCR) was defined as a serum PSA value >=0.2 ng/mL, or 2 progressively rising PSA values >0.14 ng/mL. Significant BCR (sBCR) was defined as a BCR with a PSA doubling time (PSADT) <36 months. Insignificant BCR (iBCR) was defined as BCR with a PSADT >=36 months. RESULTS: Eight hundred fifty-seven of men (48.1%) undergoing open RP had a pathologic diagnosis of Gleason 6. Twenty-three of 857 of these men (2.7%) developed BCR, 7 were designated as iBCR (mean PSADT 81 months, range 36 to 100), 16 were sBCR (mean PSADT 8 months, range 1.5-20 months). There was a 10-fold difference in PSADT between the sBCR and iBCR groups (P <.001). All men with sBCR underwent salvage radiation therapy (SRT) and all demonstrated a subsequent PSA decline to <=0.1 ng/mL, suggesting all men had local recurrence. Two men (0.23%) developed a BCR after salvage radiation therapy, both of whom were found to have Gleason 7 disease after pathologic re-review. CONCLUSION: In our large cohort of men with pathological Gleason 6 disease undergoing open RP, sBCR were attributable exclusively to local disease recurrences. Our findings support the conclusion that Gleason 6 disease exhibits a very low capacity for metastatic spread.

CDK2 and mTOR are direct molecular targets of isoangustone A in the suppression of human prostate cancer cell growth.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Donin NM; Laze J; Zhou M; Ren Q; Lepor H

INSTITUCIÓN / INSTITUTION: Department of Urology, New York University School of Medicine, New York, NY. Electronic address: Nicholas.Donin@nyumc.org.
Licorice extract which is used as a natural sweetener has been shown to possess inhibitory effects against prostate cancer, but the mechanisms responsible are poorly understood. Here, we report a compound, isoangustone A (IAA) in licorice that potently suppresses the growth of aggressive prostate cancer and sought to clarify its mechanism of action. We analyzed its inhibitory effects on the growth of PTEN-deleted human prostate cancer cells, in vitro and in vivo. Administration of IAA significantly attenuated the growth of prostate cancer cell cultures and xenograft tumors. These effects were found to be attributable to inhibition of the G1/S phase cell cycle transition and the accumulation of p27kip1. The elevated p27kip1 expression levels were concurrent with the decrease of its phosphorylation at threonine 187 through suppression of CDK2 kinase activity and the reduced phosphorylation of Akt at Serine 473 by diminishing the kinase activity of the mammalian target of rapamycin (mTOR). Further analysis using recombinant proteins and immunoprecipitated cell lysates determined that IAA exerts suppressive effects against CDK2 and mTOR kinase activity by direct binding with both proteins. These findings suggested that the licorice compound IAA is a potent molecular inhibitor of CDK2 and mTOR, with strong implications for the treatment of prostate cancer. Thus, licorice-derived extracts with high IAA content warrant further clinical investigation for nutritional sources for prostate cancer patients.
healthy volunteers, 181 patients with metastatic RCC, and 26 patients with other solid tumors in 17 trials, the disposition of axitinib was best described by a 2-compartment model with first-order absorption and a lag time, with estimated mean systemic clearance (CL) of 14.6 L/h and central volume of distribution (V©) of 47.3 L. Of 12 covariates tested, age over 60 years and Japanese ethnicity were associated with decreased CL, whereas V© increased with body weight. However, the magnitude of predicted changes in exposure based on these covariates does not warrant dose adjustments. Multivariate Cox proportional hazard regression and logistic regression analyses showed that higher exposure and diastolic blood pressure were independently associated with longer progression-free and overall survivals and higher probability of partial response in metastatic RCC patients. These findings support axitinib dose titration to increase plasma exposure in patients who tolerate axitinib, and also demonstrate diastolic blood pressure as a potential marker of efficacy.

[596]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hegde JV; Mulkern RV; Panych LP; Fennessy FM; Fedorov A; Maier SE; Tempany CM
INSTITUCIÓN / INSTITUTION: - Department of Radiology, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA 02115, USA.
RESUMEN / SUMMARY: - Magnetic resonance (MR) examinations of men with prostate cancer are most commonly performed for detecting, characterizing, and staging the extent of disease to best determine diagnostic or treatment strategies, which range from biopsy guidance to active surveillance to radical prostatectomy. Given both the exam’s importance to individual treatment plans and the time constraints present for its operation at most institutions, it is essential to perform the study effectively and efficiently. This article reviews the most commonly employed modern techniques for prostate cancer MR examinations, exploring the relevant signal characteristics from the different methods discussed and relating them to intrinsic prostate tissue properties. Also, a review of recent articles using these methods to enhance clinical interpretation and assess clinical performance is provided. J. Magn. Reson. Imaging 2013;37:1035-1054. © 2013 Wiley Periodicals, Inc.
**TÍTULO / TITLE:** - Etiological correlation of human papillomavirus infection in the development of female bladder tumor.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Shigehara K; Kawaguchi S; Sasagawa T; Nakashima K; Nakashima T; Shimamura M; Namiki M

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Ishikawa Prefectural Central Hospital, Kanazawa, Japan.

**RESUMEN / SUMMARY:** - The critical factors and etiological role of human papillomavirus (HPV) infection in the development of female bladder tumor were examined. Eighty-four female patients with primary bladder tumor were studied. After DNA extraction from each paraffin-embedded tissue, HPV-DNA and genotype were checked. In cases of all HPV-positive cases and some HPV-negative cases, in situ hybridization (ISH) for high-risk HPV-DNA, and immunohistochemical analysis for p16-INK4a were performed. HPV-DNA was detected in 5 (6.0%) of 84 eligible patients, and HPV16 was detected in 3 patients, and HPV6 and HPV52 was detected in one case, respectively. HPV-DNA was detected frequently in younger patients and in patients with a history of cervical cancer. In four high-risk HPV-positive cases, high-risk HPV-DNA was present in tumor tissues, and p16-INK4a was expressed moderately or strongly. Two cases had a past history of cervical cancer. In these 2 cases, the same HPV type (HPV16) was detected from bladder tumor and cervical cancer. High-risk HPV-DNA ISH signals and p16-INK4A expression were also detected widely in these cervical cancer tissues. HPV infection is likely to play an important role in the development of female bladder tumor at younger cases with a past history of cervical cancer.

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[598]

**TÍTULO / TITLE:** - Prostate-specific antigen (PSA) rate of decline post external beam radiotherapy predicts prostate cancer death.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Shi Z; Pinnock CB; Kinsey-Trotman S; Borg M; Moretti KL; Walsh S; Kopsaftis T

**INSTITUCIÓN / INSTITUTION:** - Discipline of Medicine, University of Adelaide, SA, Australia. Electronic address: zumin.shi@adelaide.edu.au.
RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: To assess the association between PSA velocity (PSAV) in the first 24 months after external beam radiotherapy (EBRT) and prostate cancer-specific mortality (PCSM) and all cause mortality. MATERIALS AND METHODS: All eligible patients in the South Australian (SA) Prostate Cancer Clinical Outcomes registry were followed. 848 Patients treated by definitive EBRT with more than one PSA recorded in the two year post-treatment were included. We calculated PSAV by linear regression. RESULTS: The mean number of PSA measurements in the 2-year period was 4.4 (SD1.9). The median PSAVs across quartiles (Q1-Q4) were -4.17, -1.29, -0.38 and 0.20ng/ml/yr. In multivariable analysis, a U-shaped relationship was seen between PSAV and PCSM with Q1-Q4 hazard ratios (HR) being 3.82 (1.46-10.00), 3.07 (1.10-8.58), 1, 5.15 (1.99-13.30) respectively. HR for all cause mortality in a similar model were 1.79 (1.07-2.98), 1.55 (0.93-2.59), 1.00 and 1.74 (1.04-2.90) for Q1 to Q4 respectively. A rapid PSA decline in the first year was a strong predictor of PCSM. However, in the second year PSA increase was positively associated with PCSM.

CONCLUSION: A rapid decline in PSA in the first year following EBRT is positively associated with PCSM. This may be a useful early indicator of the need for additional therapies.

[599]

TÍTULO / TITLE: - Comparison of survival analysis and palliative care involvement in patients aged over 70 years choosing conservative management or renal replacement therapy in advanced chronic kidney disease.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hussain JA; Mooney A; Russon L


RESUMEN / SUMMARY: - Background: There are limited data on the outcomes of elderly patients with chronic kidney disease undergoing renal replacement therapy or conservative management. Aims: We aimed to compare survival, hospital admissions and palliative care access of patients aged over 70 years with chronic kidney disease stage 5 according to whether they chose renal replacement therapy or conservative management. Design: Retrospective observational study. Setting/participants: Patients aged over 70 years attending pre-dialysis clinic. Results: In total, 172 patients chose conservative management and 269 chose renal replacement therapy. The renal replacement therapy group survived for longer when survival was taken from the time estimated glomerular filtration rate <20 mL/min (p < 0.0001), <15 mL/min (p < 0.0001) and <12 mL/min (p = 0.002). When factors influencing survival were stratified...
for both groups independently, renal replacement therapy failed to show a survival advantage over conservative management, in patients older than 80 years or with a World Health Organization performance score of 3 or more. There was also a significant reduction in the effect of renal replacement therapy on survival in patients with high Charlson’s Comorbidity Index scores. The relative risk of an acute hospital admission (renal replacement therapy vs conservative management) was 1.6 (p < 0.05; 95% confidence interval = 1.14-2.13). A total of 47% of conservative management patients died in hospital, compared to 69% undergoing renal replacement therapy (Renal Registry data). Seventy-six percent of the conservative management group accessed community palliative care services compared to 0% of renal replacement therapy patients.Conclusions: For patients aged over 80 years, with a poor performance status or high co-morbidity scores, the survival advantage of renal replacement therapy over conservative management was lost at all levels of disease severity. Those accessing a conservative management pathway had greater access to palliative care services and were less likely to be admitted to or die in hospital.

[600]
TÍTULO / TITLE: - Imaging-guided radiofrequency ablation of cystic renal neoplasms.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 2214/AJR.12.9336
AUTORES / AUTHORS: - Allen BC; Chen MY; Childs DD; Zagoria RJ
INSTITUCIÓN / INSTITUTION: - 1 Department of Radiology, Wake Forest Baptist Medical Center, Medical Center Blvd, 3rd Fl MRI, Winston-Salem, NC 27157-1088.
RESUMEN / SUMMARY: - OBJECTIVE. The purpose of this article is to determine whether percutaneous radiofrequency ablation (RFA) is effective and safe for the treatment of cystic renal neoplasms. MATERIALS AND METHODS. This is a retrospective review of imaging-guided RFA of Bosniak III and IV cysts from one institution. Thirty-eight subjects (19 men and 19 women; mean age, 71 years; age range, 46-95 years) underwent RFA of 40 cystic neoplasms (Bosniak III, n = 25; Bosniak IV, n = 15). Percutaneous biopsy was performed in 90% (36/40) of lesions. For patients with imaging follow-up of at least 1 year (n = 21), the mean duration of surveillance was 2.8 years (range, 1-6.5 years). The electronic medical record was reviewed for complications related to the procedure. Estimated glomerular filtration rate (GFR) was measured before RFA and at the last follow-up visit more than 6 months after the RFA session. RESULTS. According to percutaneous biopsy, 61.1% (22/36) of lesions were
malignant, and 38.9% (14/36) of biopsies were inconclusive. There was no local tumor progression, and no subjects developed metastatic disease. One subject developed a new solid renal mass during the course of follow-up. Minor complications occurred in 5.3% (2/38) of ablations and included dysuria and mild hydronephrosis related to a blood clot in the ureter. There was one major complication (2.6%), a case of flash pulmonary edema. On average, estimated GFR decreased by 2.5 mL/min/1.73 m². CONCLUSION. Imaging-guided RFA is an effective and safe treatment of Bosniak III and IV cystic renal neoplasms with outcomes comparable to those of surgical therapies.

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[601]

**TÍTULO / TITLE:** Hypoxia-inducible factor 1alpha mediates the down-regulation of superoxide dismutase 2 in von Hippel-Lindau deficient renal clear cell carcinoma.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Gao YH; Li CX; Shen SM; Li H; Chen GQ; Wei Q; Wang LS

**INSTITUCIÓN / INSTITUTION:** Shanghai Universities E-Institute for Chemical Biology, Key Laboratory of Cell Differentiation and Apoptosis of National Ministry of Education, Shanghai Jiaotong University School of Medicine (SJTU-SM), Shanghai 200025, PR China.

**RESUMEN / SUMMARY:** Hypoxia-inducible factor 1alpha (HIF-1alpha) is an oxygen-sensitive subunit of HIF-1, the master transcription factor for cellular response to hypoxia. Down-regulation of the mitochondrial enzyme superoxide dismutase 2 (SOD2) contributes to the stabilization of HIF-1alpha under hypoxia due to the decreased dismutation of superoxide radical. Here we report that HIF-1alpha could also regulate the expression of SOD2. We found that both stabilization of HIF-1alpha expression under nomoxia caused by pVHL deficiency and hypoxia treatment significantly reduced SOD2 expression, and shRNAs specifically against HIF-1alpha restored SOD2 expression in both circumstances. Further analyses with luciferase reporter assay and chromatin immunoprecipitation assay revealed that HIF-1alpha inhibited and directly bound to the hypoxia-responsive element in SOD2 promoter. These findings indicated the existence of a positive feedback between HIF-1alpha and SOD2 and provided new clues for understanding the molecular mechanisms of hypoxia adaptation.

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[602]
TÍTULO / TITLE: - The survival benefit of lymph node dissection at the time of removal of kidney, prostate and urothelial carcinomas: what is the evidence?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Bensalah K; Roupret M; Xylinas E; Shariat S
INSTITUCIÓN / INSTITUTION: - Department of Urology, Rennes University Hospital, University of Rennes, 2, rue Henri Le Guillou, 35000, Rennes, France, Karim.bensalah@chu-rennes.fr.
RESUMEN / SUMMARY: - INTRODUCTION: Lymph node dissection (LND) has been advocated by oncologic surgeons to completely eradicate cancer. However, evidence for that strategy is solely based on poor quality data. Some randomized studies done outside the field of urology failed to show any benefit to LND. Our objective was to evaluate whether LND at the time of removal of prostate, kidney and urothelial carcinomas results in a survival benefit.
METHODS: For that purpose, we performed a systematic literature review.
RESULTS: For kidney cancer, LND might be able to cure some patients with N+ disease. In N0 patients, although a randomized trial has been completed, the value of LND remains uncertain. LND at the time of radical prostatectomy can be useful in some patients with lymph node invasion. However, studies on the impact of LND in pN0 patients are retrospective and conflictive. Extended LND has been recommended when performing a radical cystectomy based on improved outcomes observed in retrospective studies. However, these studies are limited by selection biases and results of ongoing randomized trials will specify the template and the advantages of LND when removing a bladder cancer. Recent data of large series of radical nephroureterectomies for upper tract urothelial carcinomas are conflicting. Some found a benefit of LND in N0 patients while others did not. CONCLUSION: The studies that support LND at the time of surgery for prostate, kidney and urothelial carcinomas have low level of evidence. This should encourage urologists to design and perform well-designed randomized trials to assess the potential survival impact of a commonly done procedure.

[603]
TÍTULO / TITLE: - High-risk prostate cancer: combination of high-dose, high-precision radiotherapy and androgen deprivation therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Michel B; Camille V; Jean-Alexandre L
INSTITUCIÓN / INSTITUTION: - aClinique Universitaire de Cancerologie-Radiotherapie bClinique Universitaire d’Urologie de Transplantation Renale, Grenoble, France.

RESUMEN / SUMMARY: - PURPOSE OF REVIEW: High-risk prostate cancer (PCa) harbours a risk of local, regional and systemic relapse requiring the combination of a loco-regional treatment such as external beam radiotherapy for controlling the pelvic-confined disease, combined with an androgen deprivation therapy (ADT) to potentiate irradiation and to destroy the infraclinical androgen-dependent disease outside the irradiated volume. RECENT FINDINGS: Many phase III randomized trials issued from the Radiation Therapy Oncology Group (USA) and from the EORTC Radiation Oncology Group have paved the way for establishing the indications of this combined approach. SUMMARY: For locally advanced PCa, the combination needs a long-term ADT (>/=2 years) with luteinizing hormone-releasing hormone agonists. For high-risk localized PCa, the combination requires a 6-month complete androgen blockade. Image-guided intensity-modulated radiotherapy has replaced conventional irradiation and allows a dose escalation, improving the local control without increasing the toxicity. A multidisciplinary approach will enable physicians to tailor the treatment policy and a close cooperation with general practitioners and specialists will be set up to prevent as much as possible the side-effects of ADT.

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TÍTULO / TITLE: - Paratesticular Liposarcoma: Unusual Patterns of Recurrence and Importance of Margins.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Khandekar MJ; Raut CP; Hornick JL; Wang Q; Alexander BM; Baldini EH

INSTITUCIÓN / INSTITUTION: - Harvard Radiation Oncology Program, Brigham and Women's Hospital, Boston, MA, USA.

RESUMEN / SUMMARY: - BACKGROUND: Paratesticular liposarcoma (LPS) is a rare entity for which optimal treatment has not been defined. We sought to determine recurrence patterns and prognostic factors. METHODS: A total of 25 patients with localized paratesticular LPS between 1987 and 2009 were reviewed. Actuarial local-recurrence-free survival (LRFS), disease-free-survival (DFS), and overall survival (OS) were determined using the Kaplan-Meier method. RESULTS: LPS histology was well differentiated for 10 patients (40 %), de-differentiated for 14 (56 %), and pleomorphic for 1 (4 %). Final margins were positive in 8 patients (32 %). Radiation therapy (RT) was given to 10 patients;
fields included inguinal canal +/- scrotum and low pelvis. LRFS rates at 3 and 5 years were 76 and 67%. The 3-year LRFS rates were lower in patients with positive margins compared with those with negative margins (29 vs 100%, p = .0005) and in patients with recurrent versus primary disease (38 vs 83%, p = .04). Among patients who received surgery and RT, margins remained a significant predictor of local recurrence (p = .009). Interestingly, recurrences in 4 patients tracked along gonadal vessels, and only 1 patient had a distant recurrence. OS at 5 years was 100%. CONCLUSIONS: For patients with localized paratesticular LPS, positive margins and presentation with recurrent disease are adverse prognostic factors for LRFS. LR for patients with positive margins is still high despite RT; thus aggressive surgery to attain negative margins should be attempted in all cases. The finding of regional recurrences along gonadal vessels should be validated, and imaging studies should be tailored to reflect potential patterns of disease at presentation and subsequent recurrence.

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TÍTULO / TITLE: - Fusion of planning CT and cystoscopy images for bladder tumor delineation: A feasibility study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Dees-Ribbers HM; Pos FJ; Betgen A; Bex A; Hulshof MC; Remeijer P; van Herk M
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, 1066 CX Amsterdam, The Netherlands.
RESUMEN / SUMMARY: - Purpose: Bladder tumor delineation and localization during treatment are challenging problems in radiotherapy for bladder cancer. The purpose of this study is to investigate improvement of tumor delineation by the fusion of cystoscopy images with the planning CT-scan using lipiodol markers injected around the visible tumor during cystoscopy. Methods: A registration method was developed for the fusion of cystoscopy images with a planning CT-scan and was tested on a phantom and retrospectively on the imaging data of four bladder cancer patients. For the patients, small deposits of lipiodol were injected at the visible margin of the tumor or previous transurethral resection site during cystoscopy. These deposits were clearly visible on the planning CT-scan and served as markers for both tumor delineation and image guidance of the radiotherapy treatment. Here, the markers were used for the registration of cystoscopy images with the planning CT-scan. The registration procedure works as follows: First, coarse registrations were made to orient the
cystoscopy image correctly, using the center of gravity of the markers, the center of the CT bladder, and one of N markers as fiducial points in a point matching procedure. Starting from these N orientations, full registrations are performed taking lens deformation into account. Since a cystoscopy image is 2D, each pixel corresponds to a line-of-sight. The distances between the CT markers and the lines-of-sight of the cystoscopy markers were minimized. The final cost function (the root mean square distance between corresponding CT markers and lines-of-sight) was used to quantify the quality of the registration. The registration with the lowest final cost was considered to represent the correct orientation. The CT-based tumor delineation was finally backprojected onto the cystoscopy image.

Results: The fusion of cystoscopy images with a planning CT-scan succeeded for the phantom and three out of four patients. The fiducial registration error (FRE) for the phantom image registration based on five markers was 1.1 mm, while the target registration error was 1.2-1.7 mm. The FREs for the patient images were 0.1-3.6 mm. The registration procedure failed for one patient, since it was not possible to indicate unambiguously the corresponding lipiodol marker locations in the cystoscopy image and the planning CT-scan. The difference between the CT and cystoscopy defined tumor outlines clearly exceeded the registration accuracy.

Conclusions: Registration of cystoscopy images and planning CT-scan is feasible and allows for improvement of tumor delineation. However, the lipiodol injection protocol needs to be improved to facilitate identification of markers on both cystoscopy images and planning CT-scans.

[606]

TÍTULO / TITLE: - A Negative Confirmatory Biopsy Among Men on Active Surveillance for Prostate Cancer Does Not Protect Them from Histologic Grade Progression.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Wong LM; Alibhai SM; Trottier G; Timilshina N; Van der Kwast T; Zlotta A; Lawrentschuk N; Kulkarni G; Hamilton R; Ferrara S; Margel D; Trachtenberg J; Jewett MA; Toi A; Evans A; Fleschner NE; Finelli A

INSTITUCIÓN / INSTITUTION: - Division of Urologic Oncology, Princess Margaret Cancer Centre, Toronto, Canada.

RESUMEN / SUMMARY: - BACKGROUND: Many men (21-52%) are reported to have no cancer on the second, also known as the confirmatory, biopsy (B2) for prostate cancer active surveillance (AS). If these men had a reduced risk of pathologic progression, particularly grade related, the intensity of their follow-up
could be decreased. OBJECTIVE: To investigate if men with no cancer on B2 are less likely to undergo subsequent pathologic progression. DESIGN, SETTING, AND PARTICIPANTS: Men were identified from our tertiary care center AS prostate cancer database (1995-2012). Eligibility criteria were prostate-specific antigen (PSA) ≤10, cT2 or lower, no Gleason grade 4 or 5, three or fewer positive cores, and no core >50% involved. Only patients with three or more biopsies were selected and then dichotomized on cancer status (yes or no) at B2. INTERVENTION: AS. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Pathologic progression was defined as grade (advancement in Gleason score) and/or volume (more than three positive cores, >50% core involved). Progression-free survival was compared. Predictors of progression were investigated using a Cox proportional hazards model. RESULTS AND LIMITATIONS: Of the 286 patients remaining on AS after B2, 149 (52%) had no cancer and 137 (48%) had cancer. The median follow-up after B2 was 41 mo (interquartile range [IQR]: 26.5-61.9). Progression-free survival at 5 yr was 85.2% versus 67.3% for negative B2 versus cancer on B2, respectively (p = 0.002). Men with no cancer at B2 had a 53% reduction in risk of subsequent progression (hazard ratio [HR]: 0.47; 95% confidence interval [CI], 0.29-0.77; p = 0.003). Subanalysis showed prognostic indicators of volume-related progression were absence of cancer (HR: 0.36; 95% CI, 0.20-0.62; p = 0.0006) and PSA density (HR: 1.79; 95% CI, 1.12-2.89; p = 0.01). The only predictor of grade-related progression was age (HR: 1.05; 95% CI, 1.00-1.10; p = 0.04). Retrospective analysis was the major limitation of the study. CONCLUSIONS: Absence of cancer on B2 is associated with a significantly decreased risk of volume-related but not grade-related progression. This must be considered when counseling men on AS.

[607]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Chapman SJ; Wah TM; Sourbron SP; Buckley DL
INSTITUCIÓN / INSTITUTION: - Division of Medical Physics, University of Leeds, Leeds, UK.
RESUMEN / SUMMARY: - AIM: To assess the effect of cryoablation on renal cell carcinoma (RCC) perfusion and single kidney (SK) glomerular filtration rate (GFR) using dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI). MATERIALS AND METHODS: Eighteen patients undergoing percutaneous cryoablation of a solitary RCC between August 2010 and November 2011 were evaluated with DCE-MRI immediately before and 1 month post-cryoablation. DCE-MRI data were acquired with 2 s temporal resolution in a coronal plane during the first pass of a 0.1 mmol/kg bolus dose of Gd-DOTA. Perfusion of the RCC (in ml/min/100 ml tissue) was estimated using a maximum slope technique. An index of SK GFR (SK-GFRi) was assessed using data acquired every 30 s for the following 3 min in the axial plane and analysed using Rutland-Patlak plots. This was compared to the GFR estimated by creatinine clearance (eGFR). RESULTS: Perfusion in the zone of ablation decreased significantly (p<0.001) from a mean of 98.0 +/- 37.5 ml/min/100 ml tissue to 11.6 +/- 4.1 ml/min/100 ml post-cryoablation; a mean decrease of 88.2%. Functional analysis was performed in seventeen patients. eGFR was underestimated by SK-GFRi which decreased significantly in tumour-bearing (-31.7%, p = 0.011), but not in contralateral kidneys (-4.4%, p = 0.14). CONCLUSION: It is feasible to measure RCC perfusion pre- and post-cryoablation using DCE-MRI. The significant decrease within the zone of ablation suggests that this technique may be useful for assessment of treatment response. Further work is required to address the underestimation of eGFR by SK-GFRi and to validate the perfusion findings.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.04.022
PURPOSE: Our aim was to screen 90 potential parameters as biomarkers of metastatic seminoma, to facilitate detection and eliminate unnecessary therapeutic or diagnostic efforts. MATERIAL AND METHODS: A total of 527 males with pure seminoma, (diagnosed 2000 - 2011), were followed during therapy. More than 90 demographic/anamnestic (e.g. age, height, weight), histopathologic parameters (testicular/tumor size, TIN), and levels of tumor markers (e.g AFP, ssHCG, LDH) in peripheral blood and testicular vein were collected for analysis via logistic regression. Previously described risk factors (tumors > 4cm, infiltration of rete testis) were assessed separately. RESULTS: Established parameters such as tumor length (p=0.0003), involvement of lymphatic (p<0.0001) or vascular channels (p=0.0009), or extent of primary tumor (p <0.0001) and infiltration of the tunica albuginea (p=0.02) and new biomarkers (absence of TIN in tumor-bearing testis [p=0.03], testicular volume [p=0.04], and tumor volume [p=0.02]) showed significant association with metastatic disease. This was also true of LDH, HCG, and AFP (p<0.0001 at maximum). However, of the discriminatory capacity of these biomarkers (concordance or ROC area) did not exceed 65% when examined either alone or in combination, and higher values (up to 80%) were detected for enzyme levels. A subset of metastatic seminoma (2-27%) was detectable with high accuracy (positive predictive value, 92-100%) based on enzyme measurements (p<0.0006). CONCLUSIONS: New biomarkers of metastatic seminoma were identified herein, and previously described risk factors were validated. Further prospective studies of these novel parameters are warranted to verify our findings and to explore a potential use for detecting occult metastases.
RESUMEN / SUMMARY: - PURPOSE: There are established variations in testicular cancer incidence between ethnic groups within countries. It is currently unclear whether occurrence of cryptorchidism - a known risk factor for testicular cancer - follows similar patterns. In New Zealand, Maori have unusually higher rates of testicular cancer than European New Zealanders, and therefore we hypothesised that ethnic trends in incidence of cryptorchidism would reflect those of testicular cancer in this context. MATERIALS AND METHODS: We tested this hypothesis by following-up eligible male neonates born in New Zealand between 2000-2010 (n=318,441) for incidence of orchidopexy-confirmed cryptorchidism and incidence of known risk factors for cryptorchidism (low birth weight, short gestation, and small size for gestational age), using routine maternity, hospitalisation and mortality records. Logistic regression was used to calculate odds ratios for the presence of known risk factors for cryptorchidism by ethnic group. Poisson regression was used to calculate relative risk of cryptorchidism by ethnicity, adjusted for risk factors. RESULTS: Ethnic patterns of cryptorchidism incidence in New Zealand closely mirrored those observed previously for testicular cancer: Maori had higher rates of cryptorchidism than all other ethnic groups, with Pacific and Asian groups having the lowest rates (incidence Rate Ratios (RR): European/Other referent; Maori adjusted RR 1.2 [95% CI 1.11-1.3]; Pacific 0.89 [0.80-0.99]; Asian 0.68 [0.59-0.79]). CONCLUSION: Since the principal risk factors for cryptorchidism occur in utero, the results of the current study strengthen the likelihood that the ethnic patterning of testicular cancer is at least partly due to risk factors which occur prior to birth.

[611]

TÍTULO / TITLE: - Thyroid-like Follicular Carcinoma of the Kidney.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Cao D
INSTITUCIÓN / INSTITUTION: - Department of PathologyKey Laboratory of Carcinogenesis and Translational Research (Department of Education)Peking University Cancer Hospital & InstituteBeijing, China.

[612]
TÍTULO / TITLE: - Re: JNK and PTEN cooperatively control the development of invasive adenocarcinoma of the prostate.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.01.065

AUTORES / AUTHORS: - Atala A

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RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2012.12.080

AUTORES / AUTHORS: - Taneja SS

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TÍTULO / TITLE: - Intercellular transfer of P-glycoprotein from the drug-resistant human bladder cancer cell line BIU-87 does not require cell-to-cell contact.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1016/j.juro.2013.04.053

AUTORES / AUTHORS: - Zhou HL; Zheng YJ; Cheng XZ; Lv YS; Gao R; Mao HP; Chen Q

INSTITUCIÓN / INSTITUTION: - Department of Urology, 1st Affiliated Hospital, Fujian Medical University, 20 Chazhong Road, Fuzhou, People’s Republic of China 350005. Electronic address: zhhllg@sina.com.

RESUMEN / SUMMARY: - PURPOSE: The efflux activity of transmembrane P-glycoprotein (P-gp) prevents a variety of therapeutic drugs from reaching lethal concentrations inside cancer cells, resulting in multidrug resistance. In this study, we investigate whether drug-resistant bladder cancer cells can transfer functional P-gp to sensitive parental cells. METHODS: Drug-sensitive bladder cancer cells (BIU-87) were co-cultured for 48 h with an adriamycin-resistant derivative of the same cell line (BIU-87/ADM) in a transwell system that prevented cell contact. The presence of P-gp in membranes of recipient cells was established using FITC, LSCM, and western blotting. P-gp mRNA levels were compared between all cell types. Rhodamine 123 efflux assay was carried out to confirm that P-gp was biologically active. RESULTS: The amount of P-gp protein in BIU-87 cells co-cultured with BIU-87/ADM was significantly higher
than in BIU-87 cells (0.44 vs. 0.25, P < 0.001) and BIU-87/H33342 cells (0.44 vs. 0.26, P < 0.001), indicating P-gp transfer. P-gp mRNA expression was significantly higher in BIU-87 ADM cells than in co-cultured BIU-87 (1.28 vs. 0.30; P < 0.001), BIU-87/H33342 (0.28), and BIU-87 cells (0.25) (P < 0.001), ruling out a genetic mechanism. After 30 minutes of efflux, the fluorescence intensity of Rh123 was significantly lower in BIU-87/ADM (5.55 vs. 51.45; P = 0.004) and co-cultured BIU-87 cells than in BIU-87 cells (14.22 vs. 51.45; P < 0.001), indicating the P-gp was functional. CONCLUSIONS: Bladder cancer cells can acquire functional P-gp through a non-genetic mechanism that does not require direct cell contact. This mechanism is thus consistent with a microparticle-mediated process.

[615]
TÍTULO / TITLE: - Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - McKiernan J; Wood CG
INSTITUCIÓN / INSTITUTION: - Department of Urology, Columbia University, New York, New York.

[616]
TÍTULO / TITLE: - Re: sunitinib malate provides activity against murine bladder tumor growth and invasion in a preclinical orthotopic model.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wood DP

[617]
TÍTULO / TITLE: - On-capillary fluorescent labeling and CE-LIF analysis of glycoforms of intact prostate-specific antigen.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Garrido-Medina R; Carlos Diez-Masa J; de Frutos M
RESUMEN / SUMMARY: - The test used in clinics as prostate cancer biomarker, based on the concentration of the glycoprotein prostate-specific antigen (PSA) in serum, leads to an elevated number of false positives. In the search for new prostate cancer biomarkers, analysis of the proportions of different groups of glycoforms of PSA is promising. Peaks of PSA, called isoforms and containing one or several glycoforms of the glycoprotein, can be separated by CE. For those samples in which PSA concentration is very low, a very sensitive detection technique, such as LIF would be required. However, CE separation of fluorescently labeled isoforms of glycoproteins is challenging. In this work three different methods of fluorescent derivatization of PSA were assayed with the aim of finding conditions allowing labeling of the glycoprotein compatible with CE resolution of its isoforms. NanoOrange, as non-covalent label, 5-(iodoacetamide) fluorescein and BODIPY® FL C1 -IA, as covalent tags of thiol groups, and Chromeo P503 as covalent tag of amino groups were tried. Only the derivatization with the P503 fluorogenic dye led to the resolution by CE-LIF of several isoforms of labeled PSA. Adapting this derivatization method to be performed on-column lead to a reduction in labeling time from 4 hours to 45 seconds. Automation of the whole analysis permitted to carry out fluorescent labeling and CE separation of PSA isoforms in less than 12 min.

[618]
TÍTULO / TITLE: - Words of wisdom: Re: Abiraterone in metastatic prostate cancer without previous chemotherapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Di Lorenzo G; Buonerba C
INSTITUCIÓN / INSTITUTION: - Genitourinary Cancer Section, Medical Oncology Division, Department of Endocrinology and Oncology, University Federico II, Napoli, Italy. giuseppedilorenzoncol@hotmail.com

[619]
TÍTULO / TITLE: - Transperineal template-guided saturation biopsy using a modified technique: outcome of 270 cases requiring repeat prostate biopsy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Enlace al texto completo (gratuito o de pago) 1111/bju.12134

AUTORES / AUTHORS: - Ekwueme K; Simpson H; Zakhour H; Parr NJ

INSTITUCIÓN / INSTITUTION: - Department of Urology, Wirral University Teaching Hospital, Wirral, UK.

RESUMEN / SUMMARY: - OBJECTIVES: To determine the incidence of prostate cancer (PCa), and pathological grade and location of PCa, using a modified transperineal template-guided saturation biopsy (TTSB). To compare the acute urinary retention (AUR) rate found using modified TTSB with that of published reports. PATIENTS AND METHODS: A total of 270 consecutive patients with persistent clinical suspicion of PCa, despite a median (range) of 2 (1-6) sets of negative transrectal ultrasonography-guided biopsies, were enrolled and prospectively studied. All underwent modified TTSB avoiding the peri-urethral area at the base of the prostate under general anaesthesia. Statistical analysis was performed using binary logistic regression to determine the prebiopsy predictors of PCa and AUR. RESULTS: The median (range) patient age was 64 (43-85) years, with a median (range) prostate-specific antigen (PSA) of 10 (1-114) ng/mL and median (range) prostate volume of 45 (17-106) mL. A mean (range) of 28 (16-43) cores were taken at modified TTSB. Prostate cancer was diagnosed in 54.8% (Gleason scores 6 in 27.7%, 7 in 43.2%, 8-10 in 29.1% of patients). The anterior third only was involved in 21%, the middle third in 6.8% and the posterior third in 8.7% of positive cases, although in 75% of positive cases there was some anterior involvement. Comparing uniquely anterior tumours with the 15.5% found uniquely in either the middle or posterior thirds, there was no significant difference between number of positive cores (2 vs 1, P = 0.091), maximum percentage core involvement (30 vs 17.5%, P = 0.315) and maximum tumour length (3.5 vs 2 mm, P = 0.092). Fourteen patients (5.2%) developed AUR. On multivariate analysis, PSA density (PSAD) and pre-TTSB PSA predicted PCa diagnosis, whilst prostate volume, prebiopsy PSA and PSAD predicted AUR. CONCLUSIONS: Modified TTSB has a high cancer yield, especially in the anterior region, in patients with previously negative histology but onward suspicion of PCa. The modified TTSB technique provides a low risk of AUR without compromising cancer yield.

[620]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


1016/j.urology.2013.01.075
**RESUMEN / SUMMARY:**

**OBJETIVO:** Comparar la cirugía laparoendoscópica de sitio único (LESS) con la laparoscopía multiporta (MPL) para nefrectomía radical y trombectomía renal (RN-RVT) debido a que los problemas continúan con respecto a la adecuación de LESS para los tumores renales avanzados. **MÉTODOS:** Iniciamos un análisis retrospectivo de 26 pacientes que llevaron a cabo RN-RVT (11 LESS, 15 MPL) entre enero de 2006 y septiembre de 2011. LESS transperitoneal se obtuvo a través de una incisión umbilical a través de la cual se insertaron todos los trocares. LESS-RN-RVT recapituló los pasos de MPL-RN-RVT, incluyendo la trombectomía estapada y la extracción del tejido intacto. Se analizaron factores demográficos y características del tumor, variables peroperatorias, complicaciones y resultados. El resultado primario fue la puntuación de dolor visual analógica en el alta. **RESULTADOS:** El seguimiento medio fue de 20.8 meses. Los 15 casos de MPL se realizaron exitosamente laparoscópicamente; 1 de los 11 casos LESS requirió inserción de un portador adicional de 5 mm en un lugar separado. No hubo diferencias demográficas significativas entre los 2 grupos. Para LESS-RN-RVT y MPL-RN-RVT, el diámetro medio del tumor fue 7.1 y 7.9 cm (P = .346), la puntuación media del RENAL nephrometry score fue 10.2 y 10.5 (P = .407), el tiempo medio de la operación fue de 147 y 161 minutos (P = .331), y la pérdida de sangre estimada fue de 122 y 170 mL (P = .282). Se observaron significativamente menores puntuaciones de dolor visual analógica al alta (1.1 vs 2.7, P = .001), consumo de narcóticos (8.3 vs 14 mg, P = .049), y estancia hospitalaria (2.6 vs 3.7 días, P = .032) para pacientes LESS vs MPL. Ambos grupos tuvieron bordes negativos. No hubo diferencias significativas en complicaciones o transfusiones o en supervivencia libre de enfermedad y supervivencia global. **CONCLUSIÓN:** LESS fue comparable a MPL-RN-RVT para parámetros peroperatorios y puede conferir beneficio con dolor y estancia hospitalaria. Se requiere más estudio para establecer el papel de LESS en el manejo de neoplasias renales con RVT.
Papel del antigeno prostatico específico ante las nuevas evidencias científicas.

**TÍTULO / TITLE:** The Role of Prostate-Specific Antigen in Light of New Scientific Evidence.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Hernandez C; Morote J; Minana B; Cozar JM

**INSTITUCIÓN / INSTITUTION:** Servicio de Urologia, Hospital General Universitario Gregorio Maranon, Madrid, España. Electronic address: chernandez.hgugm@salud.madrid.org.

**RESUMEN / SUMMARY:**

**OBJECTIVE:** Review the scientific evidence acquired in recent years on Prostate-Specific Antigen (PSA).

**ACQUISITION OF EVIDENCE:** Analysis of the available evidence on the current role of PSA, according to a panel of experts who recorded their experience on the subject.

**SUMMARY OF THE EVIDENCE:** Currently, PSA cannot be considered solely an indicator of the presence or absence of prostate cancer. Rather, the determination of PSA assists the urologist in indicating the most appropriate treatment for a patient with benign prostatic hypertrophic (BPH), as well as in suspecting a prostatic tumour when the PSA reading increases >0,3ng/ml, in patients treated with 5-alpha-reductase inhibitor, over the reading achieved at six months of having initiated this treatment. Moreover, PSA is a key factor in the follow-up of patients with prostate adenocarcinoma who undergo surgery, radiation therapy or minimally invasive techniques. PSA helps to define biochemical recurrence, suggest the existence of a local or distal recurrence and propose or rule out adjuvant therapies.

**CONCLUSIONS:** New data on the current role of PSA in the management of patients treated for BPH and/or prostate cancer should be taken into account.

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Increased expression of p21Waf1/Cip1 and JNK with costimulation of prostate cancer cell activation by an siRNA Egr-1 inhibitor.

**TÍTULO / TITLE:** Increased expression of p21Waf1/Cip1 and JNK with costimulation of prostate cancer cell activation by an siRNA Egr-1 inhibitor.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Parra E; Gutierrez L; Ferreira J

**INSTITUCIÓN / INSTITUTION:** Laboratory of Experimental Biomedicine, University of Tarapaca, Campus Esmeralda, Iquique, Chile.
RESUMEN / SUMMARY: - The p21Waf1/Cip1 protein (hereafter, p21) and the cJun N-terminal kinase (JNK) are two well-characterized cell modulators that play a crucial role in cell differentiation, senescence and apoptosis. Here, we report that transcription of the p21Waf1/Cip1 and JNK-1 genes is affected by inhibition of the early growth response-1 (Egr-1) in response to a small interfering RNA [siRNA]-Egr-1) in LNCaP and PC-3 prostate carcinoma cell lines. The expression levels of protein were determined by western blotting, and apoptosis was measured by propidium iodide staining and flow cytometric analysis. Inhibition of Egr-1, p21 and JNK-1 was carried out by siRNAs. LNCaP and PC-3 cells exhibited readily detectable Egr-1, JNK and p21, even in low serum medium without the addition of other exogenous agents. The expression of Egr-1, p21 and JNK was strongly increased after treatment of the cells with TPA, tumor necrosis factor-alpha (TNF-alpha) or arsenite. Suppression of Egr-1 expression by siRNA abrogated the ability of TPA to induce Egr-1 and JNK-1 activities, moderately increasing the p21 activity and abrogating the anti-apoptotic effect of Egr-1 observed in the prostate cancer cell lines. Moreover, blockade of p21 and JNK was unable to decrease the activity of Egr-1, while siRNA against p21 abrogated the proapoptotic effect of p21. The results demonstrated that Egr-1 acts as a key player in prostate tumor cell growth and survival, while p21 plays a key proapoptotic role in LNCaP and PC-3 prostate carcinoma cell lines.

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[624]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Autorino R; Khalifeh A; Laydner H; Samarasekera D; Rizkala E; Eyraud R; Haber GP; Stein RJ; Kaouk JH
INSTITUCIÓN / INSTITUTION: - Center for Laparoscopic and Robotic Surgery, Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH 44195, USA.
RESUMEN / SUMMARY: - OBJECTIVE: To demonstrate the feasibility, and to report our single-centre perioperative outcomes of repeat robot-assisted partial nephrectomy (RAPN). PATIENTS AND METHODS: From June 2006 to June 2012, 490 patients underwent RAPN for a renal mass at our centre. Of these patients, nine who had undergone previous ipsilateral nephron-sparing surgery (NSS) were included in the analysis. Patient charts were reviewed to obtain demographic data, preoperative surgical history, operative details, and
postoperative outcomes and follow-up data. RESULTS: In all, 12 tumours were removed in nine patients (median age 69 years; six female). A third of the operations were performed on patients with a solitary kidney. The median (range) R.E.N.A.L. nephrometry score for the resected masses was 7 (4-8). The warm ischaemia time was 17.5 min and in three of the nine patients an unclamped procedure was performed. No intraoperative complications were registered, whereas only two minor complications occurred postoperatively. There were no renal unit losses. All surgical margins were negative. There was no significant difference between mean preoperative and latest postoperative mean estimated glomerular filtration rates (70.5 vs 63.5 mL/min/1.73 m(2), P > 0.05). At a mean (sd) follow-up of 8.3 (13) months, eight of the nine patients with a pathology diagnosis of malignant neoplasm were alive and free from disease at the latest follow-up. CONCLUSION: Although technically more demanding, repeat RAPN can be safely and effectively performed in patients presenting with local recurrence after primary NSS for kidney cancer.

[625]

TÍTULO / TITLE: - Inflammatory biomarkers and emotional approach coping in men with prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hoyt MA; Stanton AL; Bower JE; Thomas KS; Litwin MS; Breen EC; Irwin MR
INSTITUCIÓN / INSTITUTION: - Department of Psychology, Hunter College, City University of New York, United States. Electronic address: michael.hoyt@hunter.cuny.edu.
RESUMEN / SUMMARY: - OBJECTIVE: Emotion-regulating coping is associated with improvements in psychological and physical health outcomes. Yet in the context of prostate cancer-related stressors, limited research has characterized associations of emotion-regulating coping processes (emotional expression, emotional processing) and inflammatory processes that are related to disease risk. This investigation examined the relation of Emotional Approach Coping (EAC) with markers of inflammation to test the hypothesis that higher EAC scores at study entry (T1) would be associated with lower proinflammatory markers four months later (T2), specifically sTNF-RII, CRP, and IL-6.
METHODS: Forty-one men (M age=66.62 years; SD=9.62) who had undergone radical prostatectomy or radiation therapy for localized prostate cancer within two years completed questionnaires, including assessments of EAC, at T1, and provided blood samples for immune assessments at T2. RESULTS: When controlling for relevant biobehavioral controls, emotional processing predicted
lower IL-6 (B=.66, p<.01), sTNF-RII (B=.43, p<.05), and CRP (B=.43, p<.10),
whereas emotional expression was significantly associated with higher levels of
sTNF-RII (B=.55, p<.05). Associations of emotional expression and IL-6 (B=.38,
p<.10), and CRP (B=.44, p<.10) approached significance. Probing interactions
of emotional processing and expression (though only approaching significance)
suggested that expression of emotion is associated with higher inflammation
(CRP and sTNF-RII) only in the context of low emotional processing.

CONCLUSIONS: Attempts at emotion regulation via emotional processing
appear to modulate inflammatory processes. Understanding, making meaning
of, and working through emotional experience may be a promising target of
intervention to reduce inflammation with potential effects on psychological and
cancer outcomes in men with prostate cancer.

[626]
TITULO / TITLE: - Tubular adenoma of the urinary tract: a newly described entity.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kao CS; Epstein JI
INSTITUCION / INSTITUTION: - Department of Pathology and Laboratory Medicine,
Indiana University School of Medicine, Indianapolis, IN 46202, USA. Electronic
address: yutkao@iupui.edu.
RESUMEN / SUMMARY: - Tubular adenomas in the urinary tract with the same
appearance as those in the gastrointestinal tract have not yet been described in
the literature. We herein report 4 cases of tubular adenomas in the urinary tract
encountered within our consult practice. This lesion was defined by the
presence of a collection of small round tubular glands with intestinal-type
epithelium showing moderate dysplasia, identical to the histology of tubular
adenomas in the intestinal tract. Patients ranged in age from 37 to 63 years
(mean, 45 years), with 3 of the 4 being male (male-to-female ratio, 3:1). The
locations were urinary bladder, prostatic urethra and ureter with hematuria,
polyps, and obstructive mass as their presentations, respectively. One lesion
was large measuring 1.4 cm associated with pseudoinvasion as well as invasive
adenocarcinoma. Immunohistochemically, the tubular adenomas stained
positive for CDX2 and CK20, while negative for GATA3 and CK7. One case
showed positive nuclear beta-catenin staining. Tubular adenoma of the urinary
tract is a rare lesion, and recognition of this entity will encourage further reports
and help to better understand the relation of tubular adenoma to concurrent and
subsequent urinary tract malignancies.

470
EBV-transformed lymphoblastoid cell lines as vaccines against cancer testis antigen-positive tumors.

Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago)

Department of Internal Medicine I, Jose Carreras Center for Immuno- and Gene Therapy, University of Saarland Medical School, 66421, Homburg, Saar, Germany, frank.neumann@uks.eu.

EBV-transformed lymphoblastoid cell lines (LCL) are potent antigen-presenting cells. To investigate their potential use as cancer testis antigen (CTA) vaccines, we studied the expression of 12 cancer testis (CT) genes in 20 LCL by RT-PCR. The most frequently expressed CT genes were SSX4 (50 %), followed by GAGE (45 %), SSX1 (40 %), MAGE-A3 and SSX2 (25 %), SCP1, HOM-TES-85, MAGE-C1, and MAGE-C2 (15 %). NY-ESO-1 and MAGE-A4 were found in 1/20 LCL and BORIS was not detected at all. Fifteen of 20 LCL expressed at least one antigen, 9 LCL expressed >/=2 CT genes, and 7 of the 20 LCL expressed >/=4 CT genes. The expression of CT genes did not correlate with the length of in vitro culture, telomerase activity, aneuploidy, or proliferation state. While spontaneous expression of CT genes determined by real-time PCR and Western blot was rather weak in most LCL, treatment with DNA methyltransferase 1 inhibitor alone or in combination with histone deacetylase inhibitors increased CTA expression considerably thus enabling LCL to induce CTA-specific T cell responses. The stability of the CT gene expression over prolonged culture periods makes LCL attractive candidates for CT vaccines both in hematological neoplasias and solid tumors.

Prognostic significance of patterns of seminal vesicle invasion in prostate cancer.


Department of Oncology and Pathology, Karolinska Institutet, Stockholm, Sweden.
RESUMEN / SUMMARY: - AIMS: We aimed to evaluate the prognostic significance of histopathological patterns of seminal vesicle invasion (SVI) after radical prostatectomy. METHODS AND RESULTS: Seminal vesicles of 1050 radical prostatectomy specimens from the Karolinska Hospital, from 1998 to 2005, were reviewed. Extraprostatic SVI was found in 60 cases (5.7%). Associations between histopathological characteristics of SVI and biochemical recurrence were analysed. The SVI component of the tumour always had a Gleason score of 7 or higher. Invasion of seminal vesicle (SV) mucosa was seen in 68.3%, and was always accompanied by muscle wall invasion. SVI was associated with biochemical recurrence [HR 1.7 (95% CI 1.1-2.6), P = 0.015], while intraprostatic SVI was not. SV mucosal invasion was associated with adverse outcome [HR 4.2 (95% CI 1.2-14.2), P = 0.021], while only 15.8% of tumours with muscle wall invasion alone recurred. Other features of SVI such as the Gleason score of the SV component, laterality, invasion route, measures of extent and local margin status in the SV did not predict outcome. CONCLUSIONS: The prognosis of patients with SVI is not uniformly poor. Invasion of the SV mucosa portends a higher risk of recurrence than invasion of the muscle wall alone. There is no evidence that other histopathological features of SVI need to be reported.

[629]

TÍTULO / TITLE: - Outcome of urinary bladder recurrence after partial cystectomy for en bloc urinary bladder adherent colorectal cancer resection.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Luo HL; Tsai KL; Lin SE; Chiang PH

INSTITUCIÓN / INSTITUTION: - Department of Urology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, Republic of China.

RESUMEN / SUMMARY: - PURPOSE: Around 10 % of colorectal cancers are locally advanced at diagnosis. There are higher incidences for sigmoid and rectal cancer adhered to urinary bladder (UB) rather than other segments of colon cancer. Surgeons often performed partial cystectomy as possible for preservation of patient’s life quality. This study investigates prognostic factors in patients who underwent bladder preservation en bloc resection for UB adherent colorectal cancer. METHODS: From 2000 to 2011, 123 patients with clinically UB involvement colorectal cancer underwent primary colorectal cancer with urinary bladder resection. Seventeen patients were excluded because of the concurrent distant metastasis at diagnosis and another 22 patients were
excluded because of total cystectomy with uretero-ileoal urinary diversion. Finally, 84 patients with clinical stage IIIC (T4bN0M0, according to AJCC 7th edition) that underwent en bloc colorectal cancer resection with partial cystectomy were enrolled into this study for further analysis. RESULTS: Preoperative colovesical fistula and positive CT result were significantly more in the urinary bladder invasion group (p = 0.043 and 0.010, respectively). Pathological UB invasion is an independent predictor of intravesical recurrence (p = 0.04; HR, 10.71; 95 % CI = 1.12 approximately 102.94) and distant metastasis (p = 0.016; HR, 4.85; 95 % CI = 1.34 approximately 17.53) in multivariate analysis. CONCLUSIONS: For bladder preservation en bloc resection of urinary bladder adherent colorectal cancer, the pathological urinary bladder invasion is significantly associated with more urinary bladder recurrence and distant metastasis. This result helps surgeons make decisions at surgical planning and establish follow-up protocol.

[630]
TÍTULO / TITLE: - Multiphasic Enhancement Patterns of Small Renal Masses (<=4 cm) on Preoperative Computed Tomography: Utility for Distinguishing Subtypes of Renal Cell Carcinoma, Angiomyolipoma, and Oncocytoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Pierorazio PM; Hyams ES; Tsai S; Feng Z; Trock BJ; Mullins JK; Johnson PT; Fishman EK; Allaf ME
INSTITUCIÓN / INSTITUTION: - James Buchanan Brady Urological Institute, Johns Hopkins Medicine, Baltimore, MD. Electronic address: philpierorazio@jhmi.edu.
RESUMEN / SUMMARY: - OBJECTIVE: To analyze the enhancement patterns of small renal masses (SRMs) during 4-phase computed tomography (CT) imaging to predict histology. METHODS: One-hundred consecutive patients with SRMs and 4-phase preoperative CT imaging, who underwent extirpative surgery with a pathologic diagnosis of renal cell carcinoma (RCC), angiomyolipoma (AML), or oncocytoma, were identified from a single institution. An expert radiologist, blinded to histologic results, retrospectively recorded tumor size, RENAL (radius, exophytic/endophytic properties of the tumor, nearness of tumor deepest portion to the collecting system or sinus, anterior/posterior descriptor, and the location relative to polar lines) nephrometry score, tumor attenuation, and the renal cortex on all 4 acquisitions (precontrast, corticomedullary, nephrogenic, and delayed density). RESULTS: Pathologic diagnoses included 48 clear-cell RCCs (ccRCCs), 22 papillary RCCs, 10 chromophobe RCCs, 13 oncocytomas, and 7 AMLs. There was no
significant difference in median tumor size (P = .8), nephrometry score (P = .98), or anatomic location (P >.2) among histologies. Significant differences were noted in peak enhancement (P < .001) and phase-specific enhancement (P < .007) by histology. Papillary RCCs demonstrated a distinct enhancement pattern, with a peak Hounsfield unit (HU) of 56, and greatest enhancement during the NG and delayed phases. The highest peak HU were demonstrated by ccRCC (117 HU) and oncocytoma (125 HU); ccRCC more often peaked in the corticomedullary phase, whereas oncocytoma peaked in the nephrogenic phase. CONCLUSION: In a series of patients with SRMs undergoing 4-phase CT, tumor histologies demonstrated distinct enhancement patterns. Thus, preoperative 4-phase CT imaging may provide useful information regarding pathologic diagnosis in patients undergoing extirpative surgery.


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Di Renzo D; Persico A; Sindici G; Lelli Chiesa P

INSTITUCIÓN / INSTITUTION: - Pediatric Surgery Unit, “G. d’Annunzio” University of Chieti, “Spirito Santo” Hospital of Pescara, Italy. Electronic address: dacia.direnzo@gmail.com.

RESUMEN / SUMMARY: - Prepubertal testicular tumors are rare, and teratoma is the second most frequent histologic type. Its typical features are those of a hard and painless scrotal mass at clinical examination, and nonhomogeneous, echoic, often with calcifications at ultrasonography. Rare but reported is the atypical presentation as a transilluminating scrotal mass, due to the presence of some internal cystic areas, detectable at ultrasonography. We report the case of an infant with a transilluminating scrotal mass, mimicking at ultrasonography and surgery a simple, fully liquid cyst, which the pathologic examination revealed to be mature cystic testicular teratoma.


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
PURPOSE: To investigate a multiparametric magnetic resonance imaging (MRI) approach comprising diffusion-weighted imaging (DWI), blood oxygen-dependent (BOLD), and dynamic contrast-enhanced (DCE) MRI for characterization and differentiation of primary renal cell carcinoma (RCC).

MATERIAL AND METHODS: Fourteen patients with clear-cell carcinoma and four patients with papillary RCC were examined with DWI, BOLD MRI, and DCE MRI at 1.5T. The apparent diffusion coefficient (ADC) was calculated with a monoexponential decay. The spin-dephasing rate R2* was derived from parametric R2* maps. DCE-MRI was analyzed using a two-compartment exchange model allowing separation of perfusion (plasma flow [FP] and plasma volume [VP]), permeability (permeability surface area product [PS]), and extravascular extracellular volume (VE). Statistical analysis was performed with Wilcoxon signed-rank test, Pearson’s correlation coefficient, and receiver operating characteristic curve analysis.

RESULTS: Clear-cell RCC showed higher ADC and lower R2* compared to papillary subtypes, but differences were not significant. FP of clear-cell subtypes was significantly higher than in papillary RCC. Perfusion parameters showed moderate but significant inverse correlation with R2*. VE showed moderate inverse correlation with ADC. FP and VP showed best sensitivity for histological differentiation.

CONCLUSION: Multiparametric MRI comprising DWI, BOLD, and DCE MRI is feasible for assessment of primary RCC. BOLD moderately correlates to DCE MRI-derived perfusion. ADC shows moderate correlation to the extracellular volume, but does not correlate to tumor oxygenation or perfusion. In this preliminary study DCE-MRI appeared superior to BOLD and DWI for histological differentiation.
Prostate cancer (PCa) is the second leading cause of cancer-related deaths in men. Studies show that consumption of polyunsaturated fatty acids (PUFA) modulates the development and progression of prostate cancer. High amounts of omega-6 fatty acids have been linked with increased prostate cancer risk, whereas omega-3 fatty acids have been shown to inhibit PCa growth. However, because omega-3 and omega-6 are both essential fatty acids and part of a complete diet, it is more relevant to determine the ideal ratio of the two that would allow patients to benefit from the therapeutic properties of omega-3 fatty acids. LNCaP prostate cancer cells were treated with dietary-based ratios of omega-6 to omega-3 PUFA under hormone-deprivation conditions, and effects on various cellular processes were determined. A low omega-6 to omega-3 PUFA ratio can delay the progression of cells toward castration-resistance by suppressing pathways involved in prostate cancer progression, such as the Akt/mTOR/NFκB axis. It also suppresses the expression of cyclin D1, and activation of caspase-3 and annexin V staining shows induction of proapoptotic events. Taken together, our data demonstrates that maintaining a low omega-6 to omega-3 fatty acids ratio can enhance efficacy of hormone ablation therapy.

[634]


Treatment of non-muscle invasive bladder cancer (NMBIC) requires direct visual appreciation of the tumor. Transurethral resection that is dependent solely on white light cystoscopy (WLC) often fails to accurately stage or completely resect NMIBC. These deficiencies of WLC are significant contributors to the high rates of recurrence and eventual progression to muscle invasive disease. This article looks at technologies that are being used in adjunct to WLC to augment the urologist’s ability to identify, stage, and treat NMIBC.
PURPOSE OF REVIEW: Although most men are diagnosed with readily curable localized prostate cancer, those with high-risk features face a significant mortality risk. Androgen deprivation therapy (ADT) is a standard adjunct to radiotherapy for high-risk prostate cancer, but its role around prostatectomy has not been as clearly defined, and concerns over cardiovascular toxicity have led to decreasing use. The use of chemotherapy for localized disease remains experimental. We review the most recently published trials of neoadjuvant or adjuvant systemic therapy for prostate cancer. RECENT FINDINGS: The optimal duration of ADT with higher dose modern radiation techniques is under active investigation, but current data support the use of longer duration as standard. Prostate-specific antigen (PSA) and MRI changes may be useful in future studies optimizing duration of neoadjuvant ADT. Two years of combined ADT after prostatectomy is associated with a lower risk of disease recurrence and better prostate cancer specific mortality than predicted. Persistence of intraprostatic androgens during neoadjuvant ADT may contribute to resistance. SUMMARY: Androgen deprivation added to definitive radiation or surgery improves outcomes for high-risk prostate cancer, although the role of chemotherapy remains undefined. Molecular classification is needed to improve risk stratification.
RESUMEN / SUMMARY: - Special AT-rich sequence-binding protein-1 (SATB1) has been recently reported to be overexpressed in various cancers and associate with the malignant behavior of cancer cells. However, the expression and potential roles of SATB1 in bladder cancer remains unclear. In the present study, SATB1 expression was analyzed in 85 archived bladder cancer specimens using immunohistochemistry and the correlations between SATB1 expression and clinicopathological parameters were evaluated. To further explore the biological functions of SATB1 in bladder cancer, siRNA knockdown was performed in 5637 and T24 bladder cancer cell lines. We then carried out CCK8 assay and examined cisplatin-induced apoptosis to address the roles of SATB1 in proliferation and apoptosis. We found that SATB1 was overexpressed in 33 of 85 (38.8 %) bladder cancer specimens. SATB1 overexpression associated with tumor grade (p = 0.002) and tumor stage (p = 0.027). SATB1 depletion in 5637 and T24 cells decreased cell proliferation while upregulating cisplatin-induced apoptosis. Further study demonstrated that SATB1 knockdown decreased cyclin D1 and cyclin E expression and upregulated caspase3 cleavage. In conclusion, SATB1 is overexpressed in bladder cancer and regulates malignant cell growth and apoptosis, which makes SATB1 a therapeutic target candidate for bladder cancer.

[637]

TÍTULO / TITLE: - Magnetic Resonance Imaging Versus Histopathology in Wilms Tumor and Nephroblastomatosis: 3 Examples of Noncorrelation.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Cox SG; Kilborn T; Pillay K; Davidson A; Millar AJ

INSTITUCIÓN / INSTITUTION: - Departments of *Paediatric Surgery daggerPaediatric Radiology double daggerNational Health Laboratory Service section signHaematology/Oncology Service, Red Cross War Memorial Children's Hospital and University of Cape Town, South Africa.

RESUMEN / SUMMARY: - Magnetic resonance imaging (MRI) has become the principal tool for Wilms tumor (WT) assessment and follow-up. MRI and histopathologic findings were not congruent in 2 of the q30 scanned patients with renal masses (2008 to 2011). Three lesions thought to be WT on MRI were found to be a sclerotic nephrogenic rest (1), cystic renal dysplasia (1), and focal chronic pyelonephritis (1). The "typical" features suggesting nephroblastomatosis and WT on MRI are unreliable and such lesions require biopsy for histopathologic diagnosis, especially when nephron-sparing surgery is necessary to preserve renal function.
Words of wisdom: Re: Objective measures of renal mass anatomic complexity predict rates of major complications following partial nephrectomy.

Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago)

Pignot G; Bessede T; Patard JJ

Department of Urology, Bicetre Hospital, Paris XI University, Le Kremlin Bicetre 94270, France. gg_pignot@yahoo.fr

Cinacalcet attenuates hypercalcemia observed in mice bearing either Rice H-500 Leydig cell or C26-DCT colon tumors.

Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago)

Colloton M; Shatzen E; Wiemann B; Starnes C; Scully S; Henley C; Martin D

Department of Metabolic Disorders, Amgen, Inc., Thousand Oaks, CA 91320, United States.

Excessive secretion of parathyroid hormone-related protein (PTHrP) by tumors stimulates bone resorption and increases renal tubular reabsorption of calcium, resulting in hypercalcemia of malignancy. We investigated the ability of cinacalcet, an allosteric modulator of the calcium-sensing receptor, to attenuate hypercalcemia by assessing its effects on blood ionized calcium, serum PTHrP, and calcium-sensing receptor mRNA in mice bearing either Rice H-500 Leydig cell or C26-DCT colon tumors. Cinacalcet effectively decreased hypercalcemia in a dose- and enantiomer-dependent manner; furthermore, cinacalcet normalized phosphorus levels, but did not affect serum PTHrP. Ribonuclease protection assay results demonstrated presence of PTHrP receptor, but not calcium-sensing receptor mRNA in C26-DCT tumors. The mechanism by which cinacalcet lowered serum calcium was investigated in parathyroidectomized rats (i.e., without PTH) made hypercalcemic by PTHrP. Cinacalcet attenuated PTHrP-mediated elevations in blood ionized calcium, which were accompanied by increased plasma calcitonin. Taken together these results suggest that the cinacalcet-mediated
decrease in serum calcium is not the result of a direct effect on tumor cells, but rather is the result of increased calcitonin release. In summary, cinacalcet effectively reduced tumor-mediated hypercalcemia and corrected hypophosphatemia in mice. Further investigation of cinacalcet for treatment of hypercalcemia of malignancy is warranted.

[640]
TÍTULO / TITLE: - Downregulation of protocadherin-10 expression correlates with malignant behaviour and poor prognosis in human bladder cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago)
1177/0300060513476989
AUTORES / AUTHORS: - Ma JG; He ZK; Ma JH; Li WP; Sun G
INSTITUCIÓN / INSTITUTION: - Department of Urology, Second Hospital of Tianjin Medical University, Tianjin, China. mjh2012cd@yahoo.com.cn
RESUMEN / SUMMARY: - OBJECTIVES: This study retrospectively evaluated the prognostic significance of downregulated protocadherin-10 (PCDH10) gene expression in bladder cancer. METHODS: To evaluate the prognostic significance of downregulated PCDH10 protein levels, immunohistochemistry was used to assess the level of PCDH10 protein in surgically-resected formalin-fixed, paraffin wax-embedded transitional cell carcinoma specimens. Relationships between PCDH10 protein levels, clinicopathological characteristics and overall survival were also evaluated. RESULTS: A total of 105 bladder transitional cell carcinoma specimens and 33 normal bladder epithelial samples were investigated using immunohistochemical staining. PCDH10 protein levels were downregulated in 63.8% (67/105) of bladder cancer specimens compared with control samples. Downregulated levels of PCDH10 were significantly associated with advanced stage, higher grade, larger tumour size, nonpapillary shape, tumour recurrence and decreased overall survival rates. Multivariate analysis indicated that downregulated PCDH10 levels were independently associated with decreased overall survival and had a relative risk of death of 4.571. CONCLUSIONS: Downregulated PCDH10 levels correlated with malignant behaviour and poor overall survival in patients with bladder cancer. Downregulated PCDH10 levels might be useful as a prognostic biomarker for bladder cancer.

[641]
TÍTULO / TITLE: - Developments in External Beam Radiotherapy for Prostate Cancer.
Prostate cancer (PC) is a radiosensitive tumor, and external beam radiotherapy (EBRT) has gained its place in the treatment of PC. The aim of this review is to provide the physician involved in the treatment of PC an overview of the current indications of EBRT, to focus on some recent developments in EBRT, and to highlight promising new indications for EBRT.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Lumen N; Ost P; Van Praet C; De Meerleer G; Villeirs G; Fonteyne V

INSTITUCIÓN / INSTITUTION: - Department of Urology, Ghent University Hospital, Ghent, Belgium.

RESUMEN / SUMMARY: - Prostate cancer (PC) is a radiosensitive tumor, and external beam radiotherapy (EBRT) has gained its place in the treatment of PC. The aim of this review is to provide the physician involved in the treatment of PC an overview of the current indications of EBRT, to focus on some recent developments in EBRT, and to highlight promising new indications for EBRT.

[642]

TÍTULO / TITLE: - Serum folate and prostate-specific antigen in the United States.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Han YY; Song JY; Talbott EO

INSTITUCIÓN / INSTITUTION: - Department of Pediatrics, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA, hany2@upmc.edu.

RESUMEN / SUMMARY: - PURPOSE: Increased evidence suggests that folate may play a significant role in cancer development. This study investigates the association between levels of serum folate and prostate-specific antigen (PSA), a biomarker for prostate cancer detection. METHODS: Using data from the 2007 to 2010 National Health and Nutrition Examination Survey, a total of 3,293 men aged 40 years and older with serum PSA and folate measures were studied. Total PSA level (tPSA) and percent free/total PSA ratio (%fPSA) were major outcomes. The alternative cutpoints were used to categorize these measures as higher risks of prostate cancer (tPSA: >/=10, >/=4, and >/=2.5 ng/ml; %fPSA: </=15 and </=5 %). Serum folate level was analyzed as continuous and as quintiles. Association between serum folate and PSA levels were evaluated by multivariate linear and logistic regressions. RESULTS: Higher serum folate levels were associated with decreased log10-transformed tPSA (beta = -0.001, p = 0.061) and increased %fPSA (beta = 0.064, p = 0.012). Adjusting for age, race/ethnicity, socioeconomic status, use of non-steroidal anti-inflammatory drugs, body mass index, and smoking status, higher serum folate (fifth quintile) was associated with lower odds of having higher tPSA.
(>/=10 ng/ml) and lower %fPSA (</=25 %): (tPSA: odds ratio, OR associated with fifth to first quintile of folate level = 0.42; 95 % confidence interval, CI = 0.21, 0.83; p for trend = 0.022 and %fPSA: OR = 0.71; 95 % CI = 0.52, 0.95; p for trend = 0.044). CONCLUSIONS: Results of this study suggest that higher folate status may be protective against elevated PSA levels among men without diagnosed prostate cancer. Additional epidemiologic studies are necessary to confirm our findings and to investigate potential mechanisms.

[643]
TITULO / TITLE: - STAT3 mediates TGF-beta1-induced TWIST1 expression and prostate cancer invasion.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

TÍTULO / TITLE: - Prostate specific antigen testing: age-related interpretation in early prostate cancer detection.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Antitumour activity of abiraterone acetate against metastatic castration-resistant prostate cancer progressing after docetaxel and enzalutamide (MDV3100).

BACKGROUND: Androgen receptor (AR) signalling remains critically important in metastatic castration-resistant prostate cancer (mCRPC) as confirmed by recent phase III trials, showing a survival advantage for abiraterone acetate and enzalutamide (MDV3100). The antitumour activity of abiraterone and prednisolone in patients pre-treated with enzalutamide is as yet unknown. PATIENTS AND METHODS: We investigated the antitumour activity of abiraterone and prednisolone in patients with mCRPC who had progressed following treatment with docetaxel (Taxotere) and enzalutamide. Clinical data were retrospectively analysed for prostate-specific antigen (PSA) and RECIST responses, clinical benefit and survival. RESULTS: Thirty-eight patients were included in the analysis. The median age was 71 years (range 52-84); metastatic sites included bone disease in 37 patients (97%), lymph nodes in 15 patients (39%) and visceral disease in 10 patients (26%). Abiraterone was well tolerated. Three patients (8%) attained a PSA response, defined as >/=50% decline in PSA confirmed after >/=4 weeks, while seven patients (18%) had a >/=30% PSA decline. The median progression-free survival (PFS) was 2.7 months (95% CI 2.3-4.1). Of the 12 patients assessable radiologically, only 1 (8%) attained a confirmed partial response. CONCLUSION: Abiraterone and
prednisolone have modest antitumour activities in patients with mCRPC pretreated with docetaxel and enzalutamide.

[646]
**Título / Title:** A gEUD-based inverse planning technique for HDR prostate brachytherapy: feasibility study.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary


**Autores / Authors:** Giantsoudi D; Baltas D; Karabis A; Mavroidis P; Zamboglou N; Tselis N; Shi C; Papanikolaou N

**Institución / Institution:** Department of Radiological Sciences, University of Texas Health Sciences Center, San Antonio, Texas 78229, USA. dgiansoudi@partners.org

**Resumen / Summary:** PURPOSE: The purpose of this work was to study the feasibility of a new inverse planning technique based on the generalized equivalent uniform dose for image-guided high dose rate (HDR) prostate cancer brachytherapy in comparison to conventional dose-volume based optimization. METHODS: The quality of 12 clinical HDR brachytherapy implants for prostate utilizing HIPO (Hybrid Inverse Planning Optimization) is compared with alternative plans, which were produced through inverse planning using the generalized equivalent uniform dose (gEUD). All the common dose-volume indices for the prostate and the organs at risk were considered together with radiobiological measures. The clinical effectiveness of the different dose distributions was investigated by comparing dose volume histogram and gEUD evaluators. RESULTS: Our results demonstrate the feasibility of gEUD-based inverse planning in HDR brachytherapy implants for prostate. A statistically significant decrease in D10 or/and final gEUD values for the organs at risk (urethra, bladder, and rectum) was found while improving dose homogeneity or dose conformity of the target volume. CONCLUSIONS: Following the promising results of gEUD-based optimization in intensity modulated radiation therapy treatment optimization, as reported in the literature, the implementation of a similar model in HDR brachytherapy treatment plan optimization is suggested by this study. The potential of improved sparing of organs at risk was shown for various gEUD-based optimization parameter protocols, which indicates the ability of this method to adapt to the user’s preferences.

[647]
**Título / Title:** Germ Cell Tumor in an Adolescent With Extensive Testicular Microlithiasis: Concerns Regarding Future Management.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago)
1016/j.urology.2013.02.011
AUTORES / AUTHORS: - Cambareri GM; Reiley EA; Hensle TW
INSTITUCIÓN / INSTITUTION: - New Jersey Medical School, University of Medicine and Dentistry of New Jersey, Newark, New Jersey. Electronic address: ginacambareri@gmail.com.
RESUMEN / SUMMARY: - We report on a 14-year-old boy with bilateral testicular microlithiasis and a right-sided testicular tumor. Tumor markers alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (beta-hCG) levels were elevated and orchiectomy revealed a mixed germ cell tumor consisting of embryonal carcinoma, yolk sac tumor, choriocarcinoma, and mature teratoma. The patient had no evidence of metastatic disease. Although there is a strong association between testicular microlithiasis and testicular tumor, the pediatric literature is varying in the recommended surveillance of these patients. The literature and management of pediatric patients with testicular microlithiasis is herein reviewed.

[648]
TÍTULO / TITLE: - Expanding the Morphologic Spectrum of Adult Biphasic Renal TumorsMixed Epithelial and Stromal Tumor of the Kidney With Focal Papillary Renal Cell Carcinoma: Case Report and Review of the Literature.
RESUMEN / SUMMARY: - Mixed epithelial and stromal tumor (MEST) is a distinctive adult biphasic neoplasm of the kidney characterized by the presence of solid and cystic areas composed of spindled stroma and epithelium lining tubules and cystic spaces respectively. Most MESTs are benign although sarcomatous transformation has rarely been reported. It has not been clearly established whether the epithelial component represents entrapped tubules or constitutes a true neoplastic component. We report an unusual case of a biphasic tumor of the kidney with a benign stroma and a focal component of papillary carcinoma arising in one of the cysts and discuss its pathogenesis.

[649]
**TÍTULO / TITLE:** - ImmunoPET Imaging of Renal Cell Carcinoma with I- and Zr-Labeled Anti-CAIX Monoclonal Antibody cG250 in Mice.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Cancer Biother Radiopharm. 2013 May 22.
  ●●Enlace al texto completo (gratuito o de pago) 1089/cbr.2013.1487

**AUTORES / AUTHORS:** - Stillebroer AB; Franssen GM; Mulders PF; Oyen WJ; van Dongen GA; Laverman P; Oosterwijk E; Boerman OC

**INSTITUCIÓN / INSTITUTION:** - 1 Department of Nuclear Medicine, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands.

**RESUMEN / SUMMARY:**

Abstract Introduction: Monoclonal antibody (mAb) cG250 recognizes carbonic anhydrase IX (CAIX), overexpressed on clear cell renal cell carcinoma (ccRCC). 124I-cG250 is currently under clinical investigation for the detection of ccRCC. However, the 124I label is rapidly excreted from the tumor cells after internalization of the radiolabeled mAb. We hypothesized that labeling cG250 with the residualizing positron emitter 89Zr would lead to higher tumor uptake and more sensitive detection of ccRCC lesions.

Materials and Methods: Nude mice with CAIX-expressing ccRCC xenografts (SK-RC-52 or NU-12) were i.v. injected with 89Zr-cG250 or 124I-cG250. To determine specificity of 89Zr-cG250 uptake in ccRCC, one control group was i.v. injected with 89Zr-MOPC21 (irrelevant mAb). PET images were acquired using a small animal PET camera and the biodistribution of the radiolabeled mAb was determined.

Results: The ccRCC xenografts were clearly visualized after injection of 89Zr-cG250 and 124I-cG250. Tumor uptake of 89Zr-cG250 was significantly higher compared with 124I-cG250 in the NU-12 tumor model (114.7%±/−25.2% injected dose per gram (%ID/g) vs. 38.2%±/−18.3%ID/g, p=0.029), but in the SK-RC-52 the difference in tumor uptake was not significant (48.7%±/−15.2%ID/g vs. 32.0%±/−22.9%ID/g, p=0.26). SK-RC-52 tumors were not visualized with 89Zr-MOPC21 (tumor uptake 3.0%ID/g).

Intraperitoneal SK-RC-52 lesions as small as 7 mm3 were visualized with 89Zr-cG250 PET.

Conclusion: ImmunoPET imaging with cG250 visualized s.c. and i.p. ccRCC lesions in murine models. This confirms the potential of cG250 immunoPET in the diagnosis and (re)staging of ccRCC. PET imaging of ccRCC tumors with 89Zr-cG250 could be more sensitive than 124I-cG250-PET.

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**TÍTULO / TITLE:** - Suppression of interactions between prostate tumor cell integrin alpha beta and endothelial ICAM-1 by simvastatin inhibits prostate cancer micrometastasis.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

  ●●Enlace al texto completo (gratuito o de pago) 1002/jcp.24381

**AUTORES / AUTHORS:** - Al-Husein B; Goc A; Somanath PR
Cancer micrometastasis relies on the ability of cancer cells to secrete angiogenic modulators, to interact with the vascular endothelium, and to overcome the resistance offered by the endothelial-barrier. Being an essential step prior to metastasis, blockage of micrometastasis can have potential applications in cancer therapy and metastasis prevention. Due to poorly known molecular mechanisms leading to micrometastasis, developing therapeutic strategies to target prostate cancer utilizing drugs that block micrometastasis is far from reality. Here we demonstrate the potential benefits of simvastatin in the inhibition of prostate cancer micrometastasis and reveal the novel molecular mechanisms underlying this process. First, we showed that simvastatin inhibited the ability of human PC3 prostate cancer cells for transendothelial migration in vitro. Second, our data indicated that simvastatin modulates the expression of tumor derived factors such as angiopoietins and VEGF-A at the mRNA and protein levels by the PC3 cells, thus preventing endothelial-barrier disruption. Third, simvastatin directly activated endothelial cells and enhances endothelial-barrier resistance. Apart from this, our study revealed that simvastatin-mediated effect on PC3 micrometastasis was mediated through inhibition of integrin alphav beta3 activity and suppression of interaction between prostate cancer cell integrin alphav beta3 with endothelial ICAM-1. © 2013 Wiley Periodicals, Inc.
primary prostatic diseases. Attention to clinical and imaging features is helpful in narrowing the differential diagnosis.
immunodeficiency mice were subjected to ultrasound treatment at various peak negative pressures (250, 570 and 750 kPa) at a center frequency of 500 kHz, different microbubble concentrations (8, 80 and 1000 μL/kg) and different radiation doses (0, 2 and 8 Gy). Twenty-four hours after treatment, tumors were excised and assessed for cell death. Histologic analyses revealed that increases in radiation dose, microbubble concentration and ultrasound pressure promoted apoptotic cell death and disruption within tumors by as much as 21%, 30% and 43%, respectively. Comparable increases in ceramide, a cell death mediator, were identified using immunohistochemistry. We also show here that even clinically used microbubble concentrations combined with ultrasound can induce significant enhancement of cell death.

[654]

TÍTULO / TITLE: - ERG expression and prostatic adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Verdu M; Trias I; Roman R; Rodon N; Garcia-Pelaez B; Calvo M; Dominguez A; Banus JM; Puig X

INSTITUCIÓN / INSTITUTION: - BIOPAT, Biopatologia Molecular, Grup Assistencia, Avda. Diagonal 660, Planta -1, 08034, Barcelona, España, mverdu@histopat.es.

RESUMEN / SUMMARY: - ERG gene rearrangement has been identified as a highly specific alteration that is present in 40-50 % of prostate carcinomas. The standardization of an immunohistochemical assay with a novel anti-ERG antibody recently described would have significant diagnostic value. The aims of this study were to identify the incidence of this rearrangement in a Spanish population and to test the specificity of immunohistochemical ERG evaluation for prostate carcinomas. Three prostate tissue microarrays were constructed using radical prostatectomy specimens and related to grade, local invasion, and regional invasion. In addition to samples from malignant cases (160), specimens of prostatic hyperplasia (26) and high-grade prostatic intraepithelial neoplasia (10) were included. Tissue microarrays of 270 samples from most common malignant tumors (breast, colon, lung, and bladder) were also tested. All were analyzed by immunohistochemistry. Seventy-five out of 154 evaluable cases (49 %) of prostate carcinoma showed ERG expression; 52/75 showed strong staining. No ERG expression was observed in any of the high-grade prostatic intraepithelial neoplasia. ERG expression was independent of Gleason score (p = 0.160), extent of invasion (p = 0.517), and regional lymph node involvement (p = 0.816). No ERG expression was found in any other type of tumor, with the exception of one bladder cancer sample that showed focal and
weak expression. The frequency of ERG detected in our study correlated with the results published for other Caucasian populations. Strong ERG protein expression was exclusively detected in prostate carcinomas, corroborating the specificity of ERG rearrangements for these tumors. Thus, detecting ERG using immunohistochemistry may be useful in routine practice in pathology departments.

[655]

**TÍTULO / TITLE:** - Simultaneous and combined detection of multiple tumor biomarkers for prostate cancer in human serum by suspension array technology.

**RESUMEN / SUMMARY:** - Simultaneous and combined detection of multiple tumor biomarkers for prostate cancer in human serum by suspension array technology.


**AUTORES / AUTHORS:** - Liu N; Liang W; Ma X; Li X; Ning B; Cheng C; Ou G; Wang B; Zhang J; Gao Z

**INSTITUCIÓN / INSTITUTION:** - Tianjin Key Laboratory of Risk Assessment and Control Technology for Environment and Food Safety, Institute of Health and Environmental Medicine, Tianjin 300050, PR China.

**RESUMEN / SUMMARY:** - Tumor markers (TMs) play an important role in clinical rapid screening and diagnosis for prostate cancer (PCa). In this study, we describe a competitive method to establish the multiplex suspension array by tumor biomarkers coated on distinguishable microbeads which competing with free biomarkers for their complementary antibodies (Ab) in one single reaction system for simultaneous and combined detection of prostate TMs in human serum. The volumes of the targets coupled onto the beads and their complementary Abs were optimized. The suspension array standard curves correlated well with PCa biomarkers (R(2)>0.9968). PCa biomarker levels were quantified using median fluorescent intensities. The working ranges of prostate-specific antigen (PSA), prostate stem cell antigen (PSCA), prostate-specific membrane antigen (PSMA) and prostatic acid phosphatase (PAP) were 0.47-502.9, 1.00-923.35, 1.00-524.79, and 1.73-176.07ngmL(-1) in serum samples, respectively. This method was compared to indirect competitive enzyme linked immunosorbent assay. It was found that high concordance between the two technologies resulted from serum samples of the eight PCa patients. The multiplex suspension array technology is specific to PCa biomarkers, displayed no significant cross-reactivity, and remains stable for 6 months. We also characterized the bead surface microstructures under different conditions employing a field emission scanning electron microscope. The suspension array is a straightforward and reliable method for analysis of multiple TMs with simple operation, high sensitivity at a low cost.
### Castellano - CARCINOMA NEUROENDOCRINO DE CELULA GRANDE PROSTATICO. A PROPOSITO DE UN CASO.

**TÍTULO / TITLE:** Carcinoma neuroendocrino de celula grande prostatico. A proposito de un caso.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Moratalla Charcos LM; Pastor Navarro T; Cortes Vizcaino V; Osca Garcia JM; Gil Salom M

**INSTITUCIÓN / INSTITUTION:** Urology Department. Hospital Universitario Dr.Peset. Valencia. Spain.

**RESUMEN / SUMMARY:**

**OBJECTIVE:** To report a case of a neuroendocrine differentiation in a prostate cancer patient, a rare subtype.

**METHODS:** We describe the case of a patient diagnosed with adenocarcinoma of the prostate initially, who presented hematuria due to disease progression with neuroendocrine differentiation despite androgen-deprivation therapy (ADT).

**DISCUSION:** Prostate cancer is the most common tumor in men. Histologically they are diagnosed as adenocarcinomas, which followed by ADT for a long time, develop neuroendocrine differentiation (NED). **CONCLUSION:** The prognostic significance of NED remains controversial. We must think in neuroendocrine differentiation in ADT-treated patient with disease progression and low PSA.

### Castellano - RABDOMIOSARCOMA PARATESTICULAR: A PROPOSITO DE UN CASO.

**TÍTULO / TITLE:** Rabdomiosarcoma paratesticular: a proposito de un caso.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Pastor Navarro T; Verges Prosper A; Planelles Gomez J; Perez Ebri ML; Llorente Domenech R; Osca Garcia JM; Gil Salom M

**INSTITUCIÓN / INSTITUTION:** Urology Department. University Hospital Doctor Peset. Valencia. España.

**RESUMEN / SUMMARY:**

**OBJECTIVE:** To report a case of paratesticular rhabdomyosarcoma and to perform a bibliographic review.

**METHODS:** We report the case of a 16-year-old male referred to our Department because of a left paratesticular hard tumor with progressive growth. Ultrasound examination showed a paratesticular heterogeneous mass with Internal flow on Doppler.

**RESULTS:** The patient underwent left inguinal orchiectomy, with pathological
diagnosis of rhabdomyosarcoma. He refused adjuvant chemotherapy. After being disease-free for 13 months, he presented with left colic pain. Ultrasound and CT examinations showed a left paraaortic retroperitoneal mass causing grade III ureterohydronephrosis, and lung metastases. Despite rescue chemotherapy treatment, there was no response and the abdominal mass progressed. A surgical approach was not possible since patient showed a rapid clinical worsening leading to his death a few weeks later.

CONCLUSIONS: Paratesticular sarcomas are very uncommon tumors with poor prognosis.

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RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
baseline imaging was compared for different subgroups according to PSA level (4-10, 10-20, and >20 ng/mL), prostate volume (<35, 35-50, 50-65, and >65 mL), and PSA density (<0.15, 0.15-0.30, 0.30-0.50, and >0.50). Results- In total, 413 sites were malignant in 78 patients. By biopsy site, the accuracy was greater for contrast-tuned imaging than for baseline imaging in all PSA level, prostate volume, and PSA density subgroups except 0.30 to 0.50 (all P < .05). Contrast-tuned imaging had significantly higher sensitivity in the subgroups with PSA levels between 4 and 20 ng/mL, prostate volumes between 35 and 65 mL, and PSA densities between 0.15 and 0.50 than baseline imaging (all P < .05); it also had significantly higher specificity for all PSA level subgroups except 10 to 20 ng/mL, all prostate volume subgroups except 35 to 50 mL, and all PSA density subgroups except 0.30 to 0.50 (all P < .05). Conclusions- Contrast-tuned imaging could improve cancer detection over baseline imaging in patients with different PSA levels, prostate volumes, and PSA densities.

[660]
TITULO / TITLE: Renal Rhabdomyosarcoma in a Pancake Kidney.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
1016/j.urology.2013.03.003
AUTORES / AUTHORS: Walther A; Cost NG; Garrison AP; Geller JI; Alam S; Tiao GM
INSTITUCION / INSTITUTION: Division of Pediatric Surgery of Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.
RESUMEN / SUMMARY: Renal rhabdomyosarcoma (RMS) is a rare pediatric tumor. Pancake kidneys are unusual anatomic anomalies resulting when both upper and lower poles of the embryonic kidney become fused. We report on a 4-year-old boy who was discovered to have a stage 4, group IV renal embryonal RMS arising from a pancake kidney with metastases to the lung, pelvis, and bone marrow. Treatment included multimodal therapy, consisting of neoadjuvant chemotherapy, complete surgical resection, and adjuvant chemotherapy. He remains in clinical remission 7 months after resection.

[661]
TITULO / TITLE: Mucinous adenocarcinoma of the renal pelvis masquerading as xanthogranulomatous pyelonephritis.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
Enlace al texto completo (gratuito o de pago)

1016/j.urology.2013.03.005

AUTORES / AUTHORS: Chang CP; Wang SS; Wen MC; Ou YC

INSTITUCIÓN / INSTITUTION: Division of Urology, Department of Surgery, Taichung Veterans General Hospital, Taichung City, Taiwan.

RESUMEN / SUMMARY: Primary adenocarcinoma of the renal pelvis accounts for less than 1% of renal pelvis tumors. We encountered a patient who presented with long-term nephrolithiasis and hydronephrosis. The initial impression was xanthogranulomatous pyelonephritis. The postoperative histopathologic report showed mucinous adenocarcinoma of the renal pelvis with signet ring cell formation. Signet ring cell phenomenon is extremely rare in this kind of tumor. We describe the patient’s clinical presentation, imaging findings, histopathologic examination, and immunohistochemistry results.

Enlace al texto completo (gratuito o de pago)

[662]

TÍTULO / TITLE: Antitumoral effects of vasoactive intestinal peptide in human renal cell carcinoma xenografts in athymic nude mice.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Vacas E; Arenas MI; Munoz-Moreno L; Bajo AM; Sanchez-Chapado M; Prieto JC; Carmena MJ

INSTITUCIÓN / INSTITUTION: Department of Systems Biology, Unit of Biochemistry and Molecular Biology, University of Alcala, 28871 Alcala de Henares, España.

RESUMEN / SUMMARY: We studied antitumor effect of VIP in human renal cell carcinoma (RCC) (A498 cells xenografted in immunosuppressed mice). VIP-treated cells gave resulted in p53 upregulation and decreased nuclear beta-catenin translocation and NFkappaB expression, MMP-2 and MMP-9 activities, VEGF levels and CD-34 expression. VIP led to a more differentiated tubular organization in tumours and less metastatic areas. Thus, VIP inhibits growth of A498-cell tumours acting on the major issues involved in RCC progression such as cell proliferation, microenvironment remodelling, tumour invasion, angiogenesis and metastatic ability. These antitumoral effects of VIP offer new therapeutical possibilities in RCC treatment.

Enlace al texto completo (gratuito o de pago)

[663]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.eururo.2013.03.019
AUTORES / AUTHORS: - Cooperberg MR
INSTITUCIÓN / INSTITUTION: - University of California, San Francisco, Urology, 3025 Scott St., San Francisco, CA 94123, USA. mcooperberg@gmail.com

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.acuro.2013.01.004
AUTORES / AUTHORS: - Castillo OA; Landerer E; Vidal-Mora I
INSTITUCIÓN / INSTITUTION: - Departamento de Urología, Clínica Indisa, Santiago, Chile; Facultad de Medicina, Universidad Andres Bello, Santiago, Chile. Electronic address: octavio.castillo@indisa.cl.
RESUMEN / SUMMARY: - INTRODUCTION: Open lumbar-aortic lymphadenectomy (OLAL) is the gold standard for treating post-chemotherapy retroperitoneal masses. Laparoscopic OLAL (L-OLAL) has emerged in recent years as an alternative for the handling of patients with these masses, with the additional potential benefits of minimal invasion. OBJECTIVE: To present our experience with the laparoscopic handling (L-OLAL) of residual post-chemotherapy masses in patients with advanced testicular cancer. MATERIAL AND METHODS: Between 1993 and 2009, 43 patients underwent post-chemotherapy L-OLAL. A retroperitoneal technique was employed in all patients. We assessed demographic, perioperative and pathological variables, as well as complications and follow-up. RESULTS: A unilateral dissection was performed in 17 patients, while 26 patients underwent a bilateral retroperitoneal dissection. In the first group, 4 patients relapsed. In the second group, there were no relapses. After an average follow-up of 21 months, the overall survival rate reached 95%. We recorded a rate of perioperative complications of only 9.3%. CONCLUSIONS: In experienced hands, L-OLAL is a technically feasible surgical alternative for the treatment of patients who are carriers of advanced testicular cancer with residual post-chemotherapy masses. The dissection
performed should be bilateral to avoid tumour relapses and increase the survival rate of these patients.

WHAT’S KNOWN ON THE SUBJECT? AND WHAT DOES THE STUDY ADD?: No recent advances have been made in the treatment of patients with advanced bladder cancer and, to date, targeted therapies have not resulted in an improvement in outcome. The mammalian target of rapamycin pathway has been shown to be up-regulated in bladder cancer and represents a rational target for therapeutic intervention. In the present phase II study of everolimus, one near-complete response, one partial response and several minor responses suggest that everolimus possesses biological activity in a subset of patients with bladder cancer. To maximize benefit from targeted agents such as everolimus, the preselection of patients based on molecular phenotype is required.

OBJECTIVE: To assess the efficacy and tolerability of everolimus in advanced urothelial carcinoma (UC).

PATIENTS AND METHODS: The present study comprised a single-arm, non-randomized study in which all patients received everolimus 10 mg orally once daily continuously (one cycle = 4 weeks). In total, 45 patients with metastatic UC progressing after one to four cytotoxic agents were enrolled between February 2009 and November 2010 at the Memorial Sloan-Kettering Cancer Center. The primary endpoints were 2-month progression-free survival (PFS) and the safety of everolimus, with the secondary endpoint being the response rate. A Simon minimax two-stage design tested the null hypothesis that the true two month PFS rate was ≤50%, as opposed to the alternative hypothesis of ≥70%. RESULTS: The most common grade ¾ toxicities were fatigue, infection, anaemia, lymphopaenia, hyperglycaemia and hypophosphataemia. There were two partial responses in nodal metastases, with one patient achieving a 94% decrease in target lesions and remaining on drug at 26
months. An additional 12 patients exhibited minor tumour regression. There were 23 of 45 (51%) patients who were progression-free at 2 months with a median (95% CI) PFS of 2.6 (1.8-3.5) months and a median (95% CI) overall survival of 8.3 (5.5-12.1) months. No clear association was observed between mammalian target of rapamycin pathway marker expression and 2-month PFS.

CONCLUSIONS: Although everolimus did not meet its primary endpoint, one partial response, one near-complete response and twelve minor regressions were observed. Everolimus possesses meaningful anti-tumour activity in a subset of patients with advanced UC. Studies aiming to define the genetic basis of everolimus activity in individual responders are ongoing.

[666]
**TÍTULO / TITLE:** Immunohistochemical analysis of the role and relationship between Notch-1 and Oct-4 expression in urinary bladder carcinoma.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** APMIS. 2013 Apr 18. doi: 10.1111/apm.12086.

- Enlace al texto completo (gratuito o de pago) 1111/apm.12086

**AUTORES / AUTHORS:** Abdou AG; El-Wahed MM; Kandil MA; Samaka RM; Elkady N

**INSTITUCIÓN / INSTITUTION:** Pathology Department, Faculty of Medicine, Menofiya University, Shebein Elkom, Egypt.

**RESUMEN / SUMMARY:** Most tumors contain a minor population of cancer stem cells that are responsible for tumor heterogeneity, resistance to therapy and recurrence. Oct-4 is a transcription factor responsible for self-renewal of stem cells, whereas the Notch family of receptors and ligands may play a pivotal role in the regulation of stem cell maintenance and differentiation. This study aimed at an evaluation of Oct-4 and Notch-1 expression in both carcinoma and stromal cells of 83 cases of primary bladder carcinoma and to study the relationship between them. Notch-1 was expressed in carcinoma and stromal cells of all malignant cases, where expression in both cell types was correlated with parameters indicating differentiation, such as low grade (p < 0.05) and less proliferation (p < 0.05). However, Notch-1 expression in stromal cells was associated with nodal metastasis (p = 0.016) and advanced stage (p = 0.030). 56.6 and 75.9% of carcinoma and stromal cells of malignant cases showed Oct-4 expression, respectively. Oct-4 expression in carcinoma cells or stromal cells was associated with aggressive features of bladder carcinoma, such as poor differentiation (p = 0.001), high proliferation (p < 0.001, 0.030), and liability for recurrence (p = 0.010, p < 0.001). There was an inverse relationship between Notch-1 and Oct-4 expression in carcinoma cells (p = 0.002), but stromal expression of Notch-1 was found to be associated with a nuclear pattern of Oct-4 expression in carcinoma cells (p = 0.030). Oct-4 as a stem cell marker is expressed in carcinoma cells and in stromal cells of bladder carcinoma, where
they may cooperate in the progression of bladder carcinoma by acquiring aggressive features, such as a liability for recurrence and dissemination. Notch-1 is also expressed in both carcinoma cells and stromal cells of bladder carcinoma. Although they could share in enhancing differentiation, stromal expression of Notch-1 may have a bad impact, possibly through up-regulation of the active nuclear form of Oct-4 in carcinoma cells.

[667]  
**TITULO / TITLE:** TMPRSS2-ERG rearrangement in dominant anterior prostatic tumours: incidence and correlation with ERG immunohistochemistry.  
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary  
●●Enlace al texto completo (gratuito o de pago) 1111/his.12153  
**AUTORES / AUTHORS:** Gopalan A; Leversha MA; Dudas ME; Maschino AC; Chang J; Al-Ahmadie HA; Chen YB; Tickoo SK; Reuter VE; Fine SW  
**INSTITUCIÓN / INSTITUTION:** Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.  
**RESUMEN / SUMMARY:** AIM: To study prostate cancer zonal differences in TMPRSS2-ERG gene rearrangement. METHODS AND RESULTS: We examined 136 well-characterized dominant anterior prostatic tumours, including 61 transition zone (TZ) and 75 anterior peripheral zone (PZ) lesions, defined using strict anatomical considerations. TMPRSS2-ERG FISH and ERG protein immunohistochemistry were performed on tissue microarrays. FISH results, available for 56 TZ and 71 anterior PZ samples, were correlated with ERG staining and TZ-associated ‘clear cell’ histology. Fewer TZ cancers (four of 56; 7%) were rearranged than anterior PZ cancers (18 of 71; 25%) (P = 0.009); deletion was the sole mechanism of TZ cancer rearrangement. ERG protein overexpression was present in 4% (two of 56; both FISH+) and 30% (21 of 71; 17 FISH+) of TZ and anterior PZ tumours, respectively. ‘Clear cell’ histology was present in 21 of 56 (38%) TZ and eight of 71 (11%) anterior PZ tumours. Seven per cent of cancers with and 21% without this histology had rearrangement, regardless of zonal origin. CONCLUSIONS: TMPRSS2-ERG rearrangement occurs in dominant TZ and anterior PZ prostate cancers, with all rearranged TZ cancers in this cohort showing deletion. ERG immunohistochemistry demonstrated excellent sensitivity (86%) and specificity (96%) for TMPRSS2-ERG rearrangement. TMPRSS2-ERG fusion is rare in TZ tumours and present at a low frequency in tumours displaying ‘clear cell’ histology.
**TÍTULO / TITLE:** - The Effect of Gartanin, a Naturally Occurring Xanthone in Mangosteen Juice, on the mTOR Pathway, Autophagy, Apoptosis, and the Growth of Human Urinary Bladder Cancer Cell Lines.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Liu Z; Antalek M; Nguyen L; Li X; Tian X; Le A; Zi X

**INSTITUCIÓN / INSTITUTION:** - a Department of Urology, University of California, Irvine, Orange, California, USA.

**RESUMEN / SUMMARY:** - Garcinia mangostana, often referred to as mangosteen, is a fruit grown in Southeast Asia and has been used for centuries as a local beverage and natural medicine. Its bioactive compounds, xanthones (i.e., gartanin, alpha-mangostin, etc), have reported effects on ailments ranging from skin infections and inflammation to urinary tract infections. We demonstrate that mangosteen xanthones (i.e., gartanin and alpha-mangostin) at pharmacologically achievable concentrations inhibit the growth of cancer cell lines from different stages of human urinary bladder cancer. The growth inhibitory effects of gartanin in mouse embryonic fibroblasts are at least in part dependent on the existence of p53 or TSC1. Indeed, further studies have shown that gartanin treatment of bladder cancer cell lines T24 and RT4 resulted in a marked suppression of p70S6 and 4E-BP1 expression and induction of autophagy, suggesting the inhibition of the mTOR pathway. In addition, gartanin downregulated the expression of Bcl-2 and activated the p53 pathway leading to apoptosis induction. Together, these results suggested that gartanin is a multiple targeting agent that is suitable for further study into its chemopreventive properties for human urinary bladder cancer.

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**TÍTULO / TITLE:** - Mononuclear inflammatory infiltrate and microcirculation injury in acute rejection: role in renal allograft survival.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Santos DC; Andrade LG; Carvalho MF; Neto FA; Viero RM

**INSTITUCIÓN / INSTITUTION:** - Department of Pathology, Botucatu School of Medicine, Universidade Estadual Paulista (UNESP), Botucatu, SP, Brazil.
RESUMEN / SUMMARY: - This study aimed at investigating associations between monocytes/macrophages (Mo) infiltration and three important criteria associated with acute antibody-mediated rejection: C4d staining, microcirculation injury, and graft survival time. By quantitative analysis, Mo were counted in peritubular capillaries and in the interstitial compartment (peritubular/interstitial Mo), and they were also identified in glomeruli (glomerular Mo). The study included 47 patients who received renal allograft between 1991 and 2009. Capillaritis and glomerulitis were classified by the Banff scoring system, and C4d and Mo were analyzed by immunohistochemistry. In the quantitative analysis, the mean values of 50 Mo per 10 high-power fields (HPF) and 4 Mo per glomerulus were used as cut-off points for the peritubular/interstitial and glomerular compartments, respectively. Positive C4d cases were associated with the groups of biopsies with a mean value >/=50 Mo per 10 HPF (p = 0.01) and >/=4 Mo per glomerulus (p = 0.02). The group with a mean value >/=4 Mo per glomerulus also showed association with the presence of glomerulitis (p = 0.02). Peritubular/interstitial Mo did not associate with glomerulitis. Capillaritis did not show association with peritubular/interstitial or glomerular Mo. As regards graft survival, the infiltration of Mo in glomeruli interfered with allograft survival (p = 0.01). The group with a mean value of >/=4 glomerular Mo presented worse survival at the time of the 1-year follow-up. According to the literature, our data showed that infiltration of mononuclear cells was associated with C4d staining, microcirculation injury, and glomerulitis, in particular, and that glomerular macrophages could influence renal allograft survival.

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TÍTULO / TITLE: - 5-Aza-2'-Deoxycytidine Enhances Maspin Expression and Inhibits Proliferation, Migration, and Invasion of the Bladder Cancer T24 Cell Line.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Zhang H; Qi F; Cao Y; Zu X; Chen M; Li Z; Qi L

INSTITUCIÓN / INSTITUTION: - 1 Department of Urology, The First Affiliated Hospital of University of South China , Hengyang, Hunan Province, P.R. China .

RESUMEN / SUMMARY: - Abstract Background: Downregulation of maspin expression has been linked to bladder cancer development, and that DNA methylation may be important for regulating maspin gene activation in bladder cancer cells. Thus, we attempted to explore the effects of the DNA methyltransferase inhibitor, 5-aza-2'-deoxycytidine (5-Aza-CdR), on the maspin expression and the biological behaviors in bladder cancer T24 cells. Method: The methylation status of maspin in T24 cells was investigated by methylation-specific polymerase chain reaction (PCR). After treated with different
concentrations of 5-Aza-CdR (0, 0.25, 0.5, 1, and 2 μM), the maspin gene mRNA expression and protein expression were examined by real-time PCR and western blotting analysis. Cell proliferations were evaluated by the 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide assay. Flow cytometry was used to identify the apoptosis rates. Migration and invasive ability were determined by the transwell assay. Using the western blotting analysis, the changes of Cyclin D1, VEGF-C, VEGFR-3, MMP-2, MMP-9, caspase-3 p17, Bax, and Bcl-2 expression were measured. Results: Promoter DNA methylation of maspin was observed in T24 cells. The expression levels of maspin mRNA and protein in T24 cells were increased in a dose manner after treatment with increasing 5-Aza-CdR (p<0.05). The proliferation, migration, and invasion of cells were significantly inhibited with increasing 5-Aza-CdR, whereas the apoptosis was greatly increased (p<0.05). These were associated with the decreased ratio of Bcl-2/Bax, activation of caspase-3, and decreased expression of Cyclin D1, VEGF-C, VEGFR-3, MMP-2 and MMP-9. Conclusions: The present study demonstrates that maspin is silenced by DNA methylation in bladder T24 cells, and its expression can be reactivated by treatment with 5-Aza-CdR. 5-Aza-CdR could result in obvious inhibitions of the proliferation, migration, and invasion of T24 cells, which may serve as a potential strategy for the treatment of bladder cancer.
(MMP) expression by western blotting. Dvl2 was overexpressed in LNCaP cells compared with the AI PCa lines DU-145 and PC-3, as well as in the majority of PCa tissue specimens examined by qRT-PCR (14/27, 51.9 %). Dvl2 expression was low in all 10 BPH specimens, weakly positive in 26/104 AD PCa specimens (23.8 %), positive in 60/104 AD PCa specimens (55 %), and strongly positive in all 5 AI PCa specimens. Dvl2 expression was significantly correlated with combined Gleason score (p = 0.02), lymph node metastasis (p = 0.005), and TNM stage (p = 0.015). Silencing of Dvl2 mRNA expression significantly reduced LNCaP cell proliferation, motility, invasiveness and Wnt-3α, AR, MMP-2, and MMP-9 expression. Dvl2 may increase PCa growth and metastasis potential, possibly by upregulating Wnt-3α, AR, and MMP expression. Silencing Dvl2 expression may be an effective treatment strategy for PCa.

[672]
TÍTULO / TITLE: - Improved performance of SPECT-CT In-111 capromab pendetide by correlation with diffusion-weighted magnetic resonance imaging for identifying metastatic pelvic lymphadenopathy in prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hardie AD; Rieter WJ; Bradshaw ML; Gordon LL; Young MA; Keane TE
INSTITUCIÓN / INSTITUTION: - Medical University of South Carolina, Charleston, SC, USA, andrewdhardie@gmail.com.
RESUMEN / SUMMARY: - PURPOSE: To preliminarily evaluate the potential for an improvement in diagnostic performance by a combined interpretation of In-111 capromab pendetide single photon emission computed tomography (SPECT) including computed tomography (CT) image fusion with magnetic resonance diffusion-weighted imaging (MR-DWI) for identifying prostate cancer in pelvic lymph nodes thru correlation with histopathology. MATERIALS AND METHODS: This institutional approved, retrospective study identified patients with available histopathology of lymph nodes removed at the time of radical prostatectomy and who had undergone staging with In-111 capromab pendetide SPECT-CT and/or pelvic MRI (including DWI). The performance of In-111 capromab pendetide SPECT for identifying malignant lymph nodes was assessed. Subsequently, a combined reading of In-111 capromab pendetide SPECT and prostate MRI with DWI was performed and the performance assessed. RESULTS: 18 patients underwent In-111 capromab pendetide SPECT-CT. Of these, 12 patients had also undergone imaging with MR-DWI. In-111 capromab pendetide SPECT-CT had a sensitivity of 40.0 % and specificity of 96.7 % for identification of malignant lymph nodes. However, In-
111 capromab pendetide SPECT-CT combined with MRI with DWI had a sensitivity of 88.9% and specificity of 98.5%. CONCLUSIONS: The addition of MR-DWI to the interpretation of In-111 capromab pendetide SPECT-CT may increase the sensitivity for detecting malignant lymph nodes in prostate cancer. Future prospective evaluation of combined In-111 capromab pendetide SPECT-CT and MR-DWI is indicated and may improve clinical evaluation of nodal disease in prostate cancer.

[673]
TÍTULO / TITLE: - Segmental enhancement inversion of small renal oncocytoma: differences in prevalence according to tumor size.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 2214/AJR.12.9300
AUTORES / AUTHORS: - Woo S; Cho JY; Kim SH; Kim SY; Lee HJ; Hwang SI; Moon MH; Sung CK
INSTITUCIÓN / INSTITUTION: - 1 Department of Radiology, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 110-744, Korea.
RESUMEN / SUMMARY: - OBJECTIVE. The purpose of this study was to retrospectively assess the prevalence of segmental enhancement inversion of small renal oncocytomas according to tumor size. MATERIALS AND METHODS. Thirty-three patients (19 men, 14 women; mean age, 61 years; range, 40-74 years) with 33 oncocytomas diagnosed at surgical resection who had undergone contrast-enhanced biphasic CT between January 2000 and December 2011 were included. CT scans were analyzed by two radiologists blinded to the specifics of the pathology report for size, presence of segmental enhancement inversion, enhancement pattern, and homogeneity. Segmental enhancement inversion was present when a renal mass was divided into two differently enhanced segments in the corticomedullary phase (30-40 seconds after contrast injection) with the degree of enhancement reversed in the nephrographic phase (120-180 seconds after contrast injection). The masses were further assessed for fibrous septa, cystic change, hemorrhage, and necrosis. For statistical analysis, the Pearson chi-square test and linear regression were used to evaluate the relation between the prevalence of segmental enhancement inversion and tumor size or pathologic changes. RESULTS. The mean diameter of 33 renal oncocytomas was 2.65 cm (range, 0.8-4.8 cm). There was no significant linear trend according to size (p = 0.762), although segmental enhancement inversion was significantly (p = 0.006) more common (10/12) in tumors measuring 1.5-2.9 cm. Pathologic change was present in 14 oncocytomas. There was no significant linear trend according to
size (p = 0.068), but 2.5-cm and larger tumors had a significantly higher prevalence (57.9%) (p = 0.036). Segmental enhancement inversion was more common (13/19) in tumors without pathologic change (p = 0.024).

CONCLUSION. Segmental enhancement inversion was a characteristic finding in our series of small renal oncocytomas and was more common in tumors measuring 1.5-2.9 cm. Pathologic changes such as central scar were more common in oncocytomas larger than 2.5 cm and may be related to the low occurrence of segmental enhancement inversion.

[674]

TÍTULO / TITLE: - Systematic Review of Adrenalectomy and Lymph Node Dissection in Locally Advanced Renal Cell Carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Bekema HJ; Maclennan S; Imamura M; Lam TB; Stewart F; Scott N; Maclennan G; McClinton S; Griffiths TR; Skolarikos A; Maclennan SJ; Sylvester R; Ljungberg B; N’dow J

INSTITUCIÓN / INSTITUTION: - Department of Critical Care, University of Groningen, University Medical Centre Groningen, The Netherlands.

RESUMEN / SUMMARY: - CONTEXT: Controversy remains over whether adrenalectomy and lymph node dissection (LND) should be performed concomitantly with radical nephrectomy (RN) for locally advanced renal cell carcinoma (RCC) cT3-T4N0M0. OBJECTIVE: To systematically review all relevant literature comparing oncologic, perioperative, and quality-of-life (QoL) outcomes for locally advanced RCC managed with RN with or without concomitant adrenalectomy or LND. EVIDENCE ACQUISITION: Relevant databases were searched up to August 2012. Randomised controlled trials (RCTs) and comparative studies were included. Outcome measures were overall survival, QoL, and perioperative adverse effects. Risks of bias (RoB) were assessed using Cochrane RoB tools. Quality of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation approach. EVIDENCE SYNTHESIS: A total of 3658 abstracts and 252 full-text articles were screened. Eight studies met the inclusion criteria: six LNDs (one RCT and five nonrandomised studies [NRSs]) and two adrenalectomies (two NRSs). RoB was high across the evidence base, and the quality of evidence from outcomes ranged from moderate to very low. Meta-analyses were not undertaken because of diverse study designs and data heterogeneity. There was no significant difference in survival between the groups, even though 5-yr overall survival appears better for the RN plus LND
group compared with the no-LND group in one randomised study. There was no evidence of a difference in adverse events between the RN plus LND and no-LND groups. No studies reported QoL outcomes. There was no evidence of an oncologic difference between the RN with adrenalectomy and RN without adrenalectomy groups. No studies reported adverse events or QoL outcomes.

CONCLUSIONS: There is insufficient evidence to draw any conclusions on oncologic outcomes for patients having concomitant LND or ipsilateral adrenalectomy compared with patients having RN alone for cT3-T4N0M0 RCC. The quality of evidence is generally low and the results potentially biased. Further research in adequately powered trials is needed to answer these questions.

[675]

TÍTULO / TITLE: Xp11.2 Translocation Renal Cell Carcinoma With PSF-TFE3 Rearrangement.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Zhong M; Weisman P; Zhu B; Brascesco M; Yang Y; Linehan WM; Merino MJ; Zhang D; Rohan S; Cai D; Yang X
INSTITUCIÓN / INSTITUTION: *Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, IL parallelMount Sinai School of Medicine, New York, NY daggerDepartment of Pediatrics, University of Sao Paulo, Sao Paulo, Brazil double daggerUrologic Oncology Branch section signLaboratory of Pathology, Center for Cancer Research, National Cancer Institute, Bethesda, MD.

RESUMEN / SUMMARY: Xp11.2 translocation renal cell carcinoma (Xp11.2 RCC) is a subtype of RCC characterized by translocations involving a breakpoint at the TFE3 gene (Xp11.2). Moderate to strong nuclear TFE3 immunoreactivity has been recognized as a specific diagnostic marker for this type of tumor. However, exclusive cytoplasmic localization of a TFE3 fusion protein was reported in UOK 145 cells, a cell line derived from an Xp11.2 RCC harboring the PSF-TFE3 translocation. If reproducible using immunohistochemistry (IHC), this finding would have important implications for pathologists in the diagnosis of Xp11.2 RCC, calling into question the specificity of nuclear immunoreactivity for TFE3 in these tumors. The purpose of this study was to determine whether the above-noted cytoplasmic localization of the TFE3 fusion protein could be reproduced using IHC. UOK 145 cells and fresh frozen tissue from 2 clinical cases of Xp11.2 RCC found to harbor the PSF-TFE3 gene rearrangement (by cytogenetic testing) were collected. All samples
were subjected to histopathologic evaluation by board-certified pathologists, TFE3 IHC, reverse transcription polymerase chain reaction, and Sanger sequencing analysis. A strong nuclear TFE3 immunoreactivity was demonstrated in all samples including the UOK 145 cell line. No cytoplasmic immunoreactivity was seen. Reverse transcription polymerase chain reaction and Sanger sequencing confirmed the previously reported PSF-TFE3 gene fusion between exon 9 of PSF and exon 6 of TFE3 in the UOK 145 cell line and in one of 2 clinical cases of Xp11.2 RCC. A novel PSF-TFE3 gene fusion between exon 9 of PSF and exon 5 of TFE3 was detected in the second clinical case of Xp11.2 RCC.

[676]

TÍTULO / TITLE: - Semiquinone derivative isolated from Bacillus sp. INM-1 protects cellular antioxidant enzymes from gamma-radiation-induced renal toxicity.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Mishra S; Reddy DS; Jamwal VS; Bansal DD; Patel DD; Malhotra P; Gupta AK; Singh PK; Jawed S; Kumar R

INSTITUCIÓN / INSTITUTION: - Radiation Biosciences Division, Radiation Biotechnology Group, Institute of Nuclear Medicine and Allied Sciences, Brig. S. K. Mazumdar Road, Delhi, 110054, India.

RESUMEN / SUMMARY: - This study was focused to evaluate protection of indigenous antioxidant system of mice against gamma radiation-induced oxidative stress using a semiquinone (SQGD)-rich fraction isolated from Bacillus sp. INM-1. Male C57bl/6 mice were administered SQGD (50 mg/kg b.w.i.p.) 2 h before irradiation (10 Gy) and modulation in antioxidant enzymes activities was estimated at different time intervals and compared with irradiated mice which were not pretreated by SQGD. Compared to untreated controls, SQGD pretreatment significantly (p < 0.05) accelerates superoxide dismutase, catalase, GSH, and glutathione-S-transferase activities. Similarly, significant (p < 0.05) increase in the expression of superoxide dismutase, catalase, GSH, and glutathione-S-transferase was observed in irradiated mice pretreated by SQGD, compared to only irradiated groups. Total antioxidant status equivalent to trolox was estimated in renal tissue of the mice after SQGD administration. Significant ABTS(+) radical formation was observed in H2O2-treated kidney homogenate, due to oxidative stress in the tissue. However, significant decrease in the levels of ABTS(+) radical was observed in kidney homogenate of the mice pretreated with SQGD. Therefore, it can be concluded
that SQGD neutralizes oxidative stress by induction of antioxidant enzymes activities and thus improved total antioxidant status in cellular system and hence contributes to radioprotection.

[677]
TÍTULO / TITLE: - E-Cadherin and beta-Catenin Expression during Urothelial Carcinogenesis Induced by N -butyl- N -(4-hydroxybutyl) nitrosamine in Mice.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Vasconcelos-Nobrega C; Costa C; Vala H; Colaco A; Santos L; Lopes C; Oliveira PA
INSTITUCIÓN / INSTITUTION: - Agrarian School of Viseu, Polytechnic Institute of Viseu, Viseu, Portugal.
RESUMEN / SUMMARY: - Background: E-cadherin and beta-catenin are adhesion molecules that promote integrity and stability of the urothelium. A decrease in their expression is associated with more aggressive tumour phenotypes with the ability to invade and metastasize. Material and Methods: 45 ICR male mice were used, of which 25 received N-butyl-N-(4-hydroxybutyl)nitrosamine (0.05%) in drinking water for a period of 12 weeks. Immunohistochemical expression was evaluated in all urinary bladder preparations for E-cadherin and for beta-catenin. Results: Preneoplastic lesions showed staining patterns similar to normal urothelium. In simple and nodular hyperplasia, membrane staining was dominant (66.7-78.6 and 50-100%, respectively). In dysplasia a cytoplasmic pattern was prevalent (86.7-100%). Neoplastic lesions exhibit an abnormal staining pattern (100%) with heterogeneous staining (cytoplasmic, nuclear and membrane staining). A strong correlation was observed between both adhesion molecule staining patterns (r = 0.83; p = 0.039). Conclusions: In mice, as in humans, E-cadherin and beta-catenin are valuable tools to investigate cellular adhesion status of urothelium and can be considered as indicators of tumour aggressiveness and evolution.

[678]
TÍTULO / TITLE: - Office-based Bladder Tumor Fulguration and Surveillance: Indications and Techniques.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - O'Neil BB; Lowrance WT
INSTITUCIÓN / INSTITUTION: Division of Urology, University of Utah, Salt Lake City, UT 84132, USA.
RESUMEN / SUMMARY: This article summarizes the current literature on office-based management of low-grade, noninvasive bladder cancer. Discussion includes differences in recurrence and progression rates between neoplasm grades and stages, role of visual grading for diagnosis, cost advantages of treatment outside the operating room, and a step-by-step description of office-based procedures.

[679]
TÍTULO / TITLE: The costs of non-muscle invasive bladder cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: James AC; Gore JL

INSTITUCIÓN / INSTITUTION: Department of Urology, University of Washington, Seattle, WA 98195, USA. acjames@u.washington.edu
RESUMEN / SUMMARY: Bladder cancer is a common diagnosis, affecting 70,000 Americans each year. Because the diagnosis, management, and long-term follow-up of non-muscle invasive bladder cancer requires advanced imaging and invasive testing, economic evaluations have shown bladder cancer to be the costliest cancer to treat in the US on a per capita basis. Adjunctive tests for surveillance have not obviated the need for cystoscopy and cytology. Indirect costs to patients include loss of work, decreased productivity, and diminished quality of life associated with diagnosis, treatment, and surveillance. Improved value may be achieved with better compliance with evidence-based practices for non-muscle invasive bladder cancer care.

[680]
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Rizk T; Taslakian B; Torbey PH; Issa G; Hourani R

INSTITUCIÓN / INSTITUTION: Department of Neurosurgery, Hotel Dieu de France, Beirut, Lebanon.
TÍTULO / TITLE: - Acoustic radiation force to reposition kidney stones.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Bailey M; Wang YN; Simon JC; Cunitz BW; Harper JD; Hsi RS; Starr F; Paun M; Dunmire B; Sapozhnikov OA; Crum LA; Sorensen MD
INSTITUCIÓN / INSTITUTION: - Ctr.Industrial and Medical Ultrasound, Appl. Phys. Lab., Univ. of Washington, 1013 NE 40th St., Seattle, WA 98105bailey@apl.washington.edu.

RESUMEN / SUMMARY: - Our group has introduced transcutaneous ultrasound to move kidney stones in order to expel small stones or relocate an obstructing stone to a nonobstructing location. Human stones and metalized beads (2-8 mm) were implanted ureteroscopically in kidneys of eight domestic swine. Ultrasonic propulsion was performed using a diagnostic imaging transducer and a Verasonics ultrasound platform. Stone propulsion was visualized using fluoroscopy, ultrasound, and the ureteroscope. Successful stone movement was defined as relocating a stone to the renal pelvis, ureteropelvic junction (UPJ), or proximal ureter. Three blinded experts evaluated for histologic injury in control and treatment arms. All stones were moved. 65% (17/26) of stones/beads were moved the entire distance to the renal pelvis (3), UPJ (2), or ureter (12). Average successful procedure per stone required 14+/-8 min and 23+/-16 pushes. Each push averaged 0.9 s in duration. Mean interval between pushes was 41+/-13 s. No gross or histologic kidney damage was identified in six kidneys from exposure to 20 1-s pushes spaced by 33 s. Ultrasonic propulsion is effective with most stones being relocated to the renal pelvis, UPJ, or ureter. The procedure appears safe without evidence of injury. [Work supported by NIH DK43881, DK092197, and NSBRI through NASA NCC 9-58.].

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[682]
TÍTULO / TITLE: - Comparison of Biochemical RecurrenceFree Survival Between Periprostatic and Pelvic Lymph Node Metastases of Prostate Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Gonzalez-Roibon N; Han JS; Lee S; Feng Z; Arslankoz S; Smith N; Pierorazio PM; Humphreys E; Deweese TL; Partin AW; Bivalacqua TJ; Han M; Trock B; Netto GJ
RESUMEN / SUMMARY: - Objective. To assess the pathologic characteristics and prognostic significance of periprostatic lymph node (LN) metastasis of prostate
cancer. The latter was performed by comparing biochemical recurrence (BCR)-free survival in cases of periprostatic LN metastasis versus matched patients showing pelvic LN metastasis. Methods and Materials. We identified 15 patients who underwent radical prostatectomy in our institution (1984-2011) showing positive periprostatic and negative pelvic LN with available follow-up information (group 1). These patients were matched 1:2 to patients with positive pelvic LN (group 2) for pertinent clinicopathologic parameters. Results. Main locations of positive periprostatic LN were posterior base and mid posterolateral. Overall higher rate of positive margins, smaller LN, and metastasis size were encountered in group 1 compared with group 2. At 5 years postprostatectomy, 69% of patients in group 1 were free of BCR, whereas 26% of those in group 2 remained BCR free, suggesting that patients with periprostatic node metastasis appeared to have a lower risk of BCR. However, the difference was not statistically significant (P = .072). The same was true when adjusted for the effect of prostate-specific antigen, surgical margin status, size of LNs, size of metastasis, age, and year of surgery. Conclusion. Patients with periprostatic node metastasis may have a lower risk of BCR compared with those with metastasis to pelvic LN. Future analysis of larger cohorts will help establish the biologic significance of prostate cancer metastasis to periprostatic LN.

[683]

TÍTULO / TITLE: Primary Cilia Metaplasia in Renal Transplant Biopsies with Acute Tubular Injury.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Hayek S Md; Parasuraman R Md; Desai HS Md; Samarapungavan D Md; Li W Md; Wolforth SC Bs; Reddy GH Md; Cohn SR Md; Rocher LL Md; Dumler F Md; Rooney MT Md; Zhang PL Md

INSTITUCIÓN / INSTITUTION: Department of Anatomic Pathology.

RESUMEN / SUMMARY: Abstract Primary cilia are hair-like organelles singly distributed along the apical surface of proximal and distal nephron tubules as mechanosensors. The goal of this study was to use electron microscopy to systematically evaluate cilia changes in acute tubular injury (ATI) from both transplant and native renal biopsies. Three groups of cases were included: control group 1-native biopsies without major changes in renal tubules; study group 2-native biopsies with prominent ATI; and study group 3-renal transplant biopsies with prominent ATI (delayed renal function group). Extensive search for ciliary structures along renal tubules was conducted in each case, focused on proximal tubular areas with injured (diminished) apical microvilli. Singly located cilia were found in 3/19 specimens in control group 1, 4/18 in group 2.
(native ATI), and 6/24 in group 3 (transplant ATI). Importantly, there were clusters of cilia in proximal tubules with markedly diminished apical microvilli in 3/24 biopsies from 2 patients in group 3, but none from groups 1 and 2. The clusters of cilia ranged from 6 to 15 individual cilia along the apical surface with diminished apical microvilli. Under high magnifications, the cilia demonstrated 9 pairs of peripheral microtubules without a central pair of microtubules, consistent with primary cilia (9 + 0) rather than motile cilia (9 + 2). In summary, the authors found clusters of cilia in proximal tubules with remarkable apical microvillar injury in 3 renal transplant biopsies with ATI, implying a reactive, or repairing, process following tubular injury, thus they name this finding "cilia metaplasia".
TÍTULO / TITLE: Salvage CT-guided Transgluteal Cryoablation for Locally Recurrent Prostate Cancer: Initial Experiences.

RESUMEN / SUMMARY: Technical feasibility of a computed tomography (CT)-guided transgluteal approach for salvage cryoablation of inoperable locally recurrent prostate cancer was evaluated retrospectively. Five procedures were performed under general anesthesia in five patients previously treated with radiation therapy. Median age was 64 years, and average pretreatment prostate-specific antigen (PSA) level was 2.77 ng/dL (range, 0.56-4.23 ng/dL). Each cryoablation procedure was completed in one session. No complications were reported. Mean 3-month and 6-month PSA levels were 0.35 ng/dL (range, 0.16-0.54 ng/dL) and 0.51 ng/dL (range, 0.09-0.94 ng/dL), respectively, representing mean decreases of 84% (range, 71%-92%) and 81% (range, 78%-84%), respectively. Salvage CT-guided transgluteal cryoablation of the prostate therefore appears technically feasible.

TÍTULO / TITLE: Metanephric adenoma and solid variant of papillary renal cell carcinoma: common and distinctive features.

RESUMEN / SUMMARY: To evaluate morphological and immunohistochemical (IHC) features helpful in distinguishing metanephric adenoma (MA) from solid papillary renal cell carcinoma (s-PRCC). METHODS AND RESULTS: We present a detailed study of 21 MA and 23 s-PRCC. The
two entities exhibited significant similarities, both being well-circumscribed
tumours composed of tightly packed small cells arranged in solid sheets or ill-
defined tubules, often presenting glomeruloid bodies, psammoma bodies and
dystrophic calcification, and showing overlapping immunoreactivity for S100,
CD57 and CK7. Conversely, most MA were non-encapsulated, whereas most s-
PRCC showed a thick fibrous pseudocapsule; MA cells had scanty cytoplasm
and a high nuclear:cytoplasmic ratio in comparison to s-PRCC, where
occasional tumour cells showed abundant cytoplasm and high nuclear grade.
Polypoid branching fronds were common in MA, but absent in s-PRCC;
multifocality and papillary hyperplasia adenoma were seen only in s-PRCC. MA
were positive for WT1 and negative for EMA and alpha-methylacyl-CoA
racemase (AMACR); s-PRCC were positive for EMA and AMACR and negative
for WT1. CONCLUSIONS: Despite overlapping features, careful morphological
and architectural evaluation should result in accurate diagnosis of most MA and
s-PRCC. In challenging cases, IHC stains for WT1, EMA and AMACR may help
in distinguishing these two entities.
CONCLUSIONS: These results suggest that the hormone related molecular pathways that drive cancer progression might be different in AC and DC. The decrease in steroid synthesis related enzymes, together with up-regulation of the BCAR1-Src pathway, emphasizes the biological particularities of DC.
AUTORES / AUTHORS: - Rocha A; Malheiro J; Fonseca I; Martins LS; Dias L; Almeida M; Pedroso S; Henriques AC

INSTITUCIÓN / INSTITUTION: - Department of Nephrology, Centro Hospitalar do Porto, Porto, Portugal. Electronic address: acrisbraga@gmail.com.

RESUMEN / SUMMARY: - Malignancy is the third most cause of death among kidney transplantation recipients after cardiovascular events and infection. The aim of this study was to investigate the types of and risk factors for cancer excluding skin lesions among kidney transplantation (KT) patients in Portugal. We studied retrospectively the 1695 patients who underwent KT between 1983 and 2009. Malignancies post-KT were considered if diagnosed at least 1 year after KT. The results were compared with a group of cancer free patients. During the follow-up period to June 2010, which included a median duration of 118.49 months (interquartile range 53.34 to 182.46), 60 patients (3.5%) developed 66 malignancies, which were the cause of death in 17. Compared with patients without cancer, the affected ones were older (P < .001), and had a longer duration of graft function (P = .002). There were no significant differences regarding gender, follow-up time, acute rejection episodes, donor type, number of KT, immunosuppressive regimen. The most frequent malignancy was colorectal cancer (21.2%), followed by malignant lymphoma (16.7%) and breast cancer (13.6%). The mean age of patients at diagnosis was 53.9 +/- 11.5 years. The average time for development of a cancer was 8.3 +/- 5.7 years with 42.4% detected between 1 and 5 years. In total, 16 patients were converted to sirolimus. Patient survival was significantly lower among subjects with cancer; censored graft survival was significantly higher in this group. A multivariate logistic regression analysis identified risk factors for malignancy post-KT to be recipient age and duration of follow-up. In conclusion, our data showed a significant number of tumors that generally not described to be higher lesions among KT. We achieved an early diagnosis and a lack of impact on death-censored graft survival.

[690]

TÍTULO / TITLE: - Epithelial-mesenchymal transition-related microRNA-200s regulate molecular targets and pathways in renal cell carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Yoshino H; Enokida H; Itesako T; Tatarano S; Kinoshita T; Fuse M; Kojima S; Nakagawa M; Seki N

INSTITUCIÓN / INSTITUTION: - Department of Urology, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan.

RESUMEN / SUMMARY: - Our recent studies of microRNA (miRNA) expression signatures demonstrated that the epithelial-mesenchymal transition (EMT)-
related microRNA-200 family (miR-200s: miR-200b/c, miR-141 and miR-429) were significantly downregulated in renal cell carcinoma (RCC) and putative tumor-suppressive miRNAs in RCC. In this study, our aim was to investigate the functional significance of the miR-200s in cancer cells and to identify novel miR-200s-regulated molecular targets and pathways in RCC. Expression levels of all the miR-200s members were significantly downregulated in human RCC tissues compared with normal renal tissues. Restoration of mature miR-200s in RCC cell line resulted in significant inhibition of cell proliferation and migration, suggesting that miR-200s function as tumor suppressors in RCC. Furthermore, we utilized gene expression analysis and in silico database analysis to identify miR-200s-regulated molecular targets and pathways in RCC. The miR-200s was categorized into two groups, according to their seed sequences, miR-200b/c/429 and miR-200b/c/141. Our data demonstrated that the ‘Focal adhesion’ and ‘ErbB signaling’ pathways were significantly regulated by miR-200b/c/429 and miR-200b/c/141, respectively. The identification of novel tumor-suppressive miR-200s-regulated molecular targets and pathways has provided new insights into RCC oncogenesis and metastasis. Journal of Human Genetics advance online publication, 2 May 2013; doi:10.1038/jhg.2013.31.
BACKGROUND: Perineural invasion is discussed as a significant route of extraprostatic extension in prostate cancer (PCa). Recent in vitro studies suggested a complex mechanism of neuroepithelial interaction.

OBJECTIVE: The present study was intended to investigate whether the concept of neuroepithelial interaction can be supported by a quantitative analysis and planimetry of capsular nerves in relation to adjacent PCa foci.

DESIGN, SETTING, AND PARTICIPANTS: Whole-mount sections of the prostate were created from patients undergoing non-nerve-sparing laparoscopic radical prostatectomy. For each prostate, adjacent sections were created and stained both to identify capsular nerves (S100) and to localize cancer foci (hematoxylin and eosin). OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Computerized quantification and planimetry of capsular nerves (ImageJ software) were performed after applying a digital grid to define 12 capsular sectors. For statistical analyses, mixed linear models were calculated using the SAS 9.3 software package. RESULTS AND LIMITATIONS: Specimens of 33 prostates were investigated. A total of 1957 capsular nerves and a total capsular nerve surface area of 26.44 mm² were measured. The major proportion was found in the dorsolateral (DL) region (p<0.001). Adjacent tumor was associated with a statistically significant higher capsular nerve count compared with the capsules of tumor-free sectors (p<0.005). Similar results were shown for capsular nerve surface area (p<0.006). Subsequent post hoc analyses at the sector level revealed that the effect of tumor on capsular nerve count or nerve surface area is most pronounced in the DL region.

CONCLUSIONS: The presence of PCa foci resulted in a significantly increased capsular nerve count and capsular nerve surface area compared with tumor-free sectors. The present study supports former in vitro findings suggesting that the presence of PCa lesions may lead to complex neuroepithelial interactions resulting in PCa-induced nerve growth.

[693]

TITULO / TITLE: - Words of wisdom. Re: Radical prostatectomy versus observation for localized prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Silberstein JL; Eastham JA
Lymphadenectomy for Bladder Cancer at the Time of Radical Cystectomy.

CONTEXT: Although the importance of lymphadenectomy during radical cystectomy (RC) in high-risk non-muscle-invasive and muscle-invasive bladder cancer (BCa) is well accepted, the optimal extent of lymphadenectomy, number of lymph nodes (LNs) to be retrieved, and prognostic and therapeutic role of lymphadenectomy remain debated issues. OBJECTIVE: In this review, we summarize the existing data on the value of lymphadenectomy for staging and outcome of BCa patients undergoing RC and lymphadenectomy. EVIDENCE ACQUISITION: A systematic Medline/PubMed literature search of peer-reviewed scientific articles published from 1998 and 2012, concerning the role of lymphadenectomy in BCa patients, was carried out. The terms and permutations used were lymphadenectomy, bladder cancer/carcinoma, urothelial carcinomas, radical cystectomy, lymph node metastasis, lymph node dissection, bladder, recurrence, and survival. Selective older articles were included. EVIDENCE SYNTHESIS: Bilateral pelvic lymphadenectomy is an integral part of RC for BCa. The literature regarding the role of lymphadenectomy in BCa patients in general is retrospective, nonstandardized, and of low-level quality in regard to evidence. Prospective randomized trials designed to define the optimal template of lymphadenectomy and its impact on oncologic outcome are advocated. Some of these studies are ongoing, and their completion and analyses are necessary to resolve controversies. CONCLUSIONS: Many consistent and concordant observations, although of low level of evidence, document that the extent of lymphadenectomy may influence disease-free survival after RC independent of the status of LNs and the pathologic stage of BCa.
Lymphadenectomy standardization at the time of RC to create evidence-based guidelines is essential for further improvement of surgical quality and BCa patient survival.

[695]
TÍTULO / TITLE: - Words of wisdom: Re: Do adenocarcinomas of the prostate with Gleason Score (GS) \( \leq 6 \) have the potential to metastasize to lymph nodes?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Richards K; Eggener S
INSTITUCIÓN / INSTITUTION: - University of Chicago, Chicago, IL, USA.

[696]
TÍTULO / TITLE: - IgG and FcgammaR genotypes and humoral immunity to mucin 1 in prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Pandey JP; Namboodiri AM; Kistner-Griffin E
INSTITUCIÓN / INSTITUTION: - Department of Microbiology and Immunology, Medical University of South Carolina, Charleston, SC, USA. Electronic address: pandeyj@musc.edu.
RESUMEN / SUMMARY: - Immunoglobulin GM and KM allotypes-hereditary antigenic determinants of gamma and kappa chains, respectively-and Fcgamma receptor Ila (FcgammaRIla) and FcgammaRIIIa genes are associated with the immunobiology of several malignant diseases, but their role in humoral immunity to the tumor-associated antigen mucin 1 (MUC1) in prostate cancer has not been examined. This investigation aimed to determine whether these genes-individually or in particular epistatic combinations-contribute to the inter-individual variability in the magnitude of antibody responsiveness to MUC1 in patients with prostate cancer. We genotyped DNA from 127 Caucasian American (CA) and 76 African American (AA) patients with histologically verified adenocarcinoma of the prostate for several GM, KM, FcgammaRIla, and FcgammaRIIIa alleles by molecular methods. We also quantitated antibodies to MUC1 in the plasma from these patients by ELISA. In
CA patients, homozygosity for the valine allele at the FcgammaRIIIa locus was significantly associated with low antibody responsiveness to MUC1 (p=0.029). In AA patients, the KM 1/3 heterozygotes had significantly higher anti-MUC1 antibody levels than 1/1 and 3/3 homozygotes (p=0.044). These results, the first to implicate FcgammaRIIIa and KM loci in humoral immunity to MUC1 in prostate cancer, might be relevant to MUC1-based immunotherapy of this malignancy.

[697]

**TÍTULO / TITLE:** - Prolonged exposure to tyrosine kinase inhibitors or early use of everolimus in metastatic renal cell carcinoma: are the two options alike?

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Calvani N; Morelli F; Chiuri V; Gnoni A; Scavelli C; Fedele P; Orlando L; Maiello E; Lorusso V; Cinieri S

**INSTITUCIÓN / INSTITUTION:** - Medical Oncology Division and Breast Unit, Sen. Antonio Perrino Hospital, S.S. 7, 72100 Brindisi, Italy.

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**RESUMEN / SUMMARY:** - We retrospectively analyzed metastatic renal cell carcinoma (RCC) patients treated with 3 targeted agents. Patients started the sequence with a tyrosine kinase inhibitor (TKI), sunitinib or sorafenib, and were divided into 2 groups based on the order in which they received the other reciprocal TKI and everolimus (EVE): TKI-TKI-EVE group (n = 19) and TKI-EVE-TKI group (n = 14). Median progression-free survival (PFS) with first TKI was 13 months in the TKI-TKI-EVE group and 10 months in the TKI-EVE-TKI group. PFS with the second agent showed a trend in favor of the TKI-TKI-EVE sequence, with a median of 11 versus 6.5 months, whereas median PFS with the third agent was 6 months in both groups. Total PFS also showed a trend in favor of the TKI-TKI-EVE sequence with a median of 31 versus 23 months. Median overall survival (OS) was 38 months in both groups, with more patients receiving subsequent treatment in the TKI-EVE-TKI group. The subgroup of patients no long-term responders (</=9 months) to first TKI showed similar outcomes irrespective of the sequence. The subgroup of long-term responders to first TKI (>9 months) who received the other TKI instead of EVE had better outcomes in terms of median PFS with the second agent (13 vs. 5.5 months; p = 0.0271), median total PFS (39.5 vs. 23.5 months; p = 0.0415), and median OS (46 vs. 38 months). In conclusion, no apparent advantage was observed with early use of EVE in advanced RCC, even in those patients who did not
benefit long from first-line TKI, whereas long-term duration of first-line TKI seems to be predictor of second-line TKI efficacy.

[698] TÍTULO / TITLE: - Testicular cancer: what the radiologist needs to know.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 2214/AJR.12.10319
AUTORES / AUTHORS: - Kreydin EI; Barrisford GW; Feldman AS; Preston MA
INSTITUCIÓN / INSTITUTION: - 1 All authors: Department of Urology, Massachusetts General Hospital, Harvard Medical School, GRB 1102, 55 Fruit St, Boston, MA 02114.
RESUMEN / SUMMARY: - OBJECTIVE. The purpose of this article is to review current imaging techniques and evolving technologies that are being used for detection and management of testicular cancer. CONCLUSION. The primary goal of cancer imaging is accurate disease characterization at diagnosis and through all stages of management. Knowledge of the disease and diagnostic performance characteristics of each technique is critical to identify the appropriate modality for staging disease and to monitor for treatment response and recurrence that may dictate further intervention.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1016/j.ijpharm.2013.04.058
AUTORES / AUTHORS: - Neutsch L; Wambacher M; Wirth EM; Spijker S; Kahlig H; Wirth M; Gabor F
INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical Technology and Biopharmaceutics, University of Vienna, Althanstrasse 14, Vienna A 1090, Austria.
RESUMEN / SUMMARY: - The urgent demand for more potent treatment schedules in bladder cancer (BCa) therapy calls for a refinement of the intravesical administration modalities. However, progress on drug delivery systems tailored to the penetration-hostile urothelial barrier lags behind the advancements in comparable fields. This study reports on a multimodal, carrier-based delivery concept that combines biorecognitive targeting with
modified release strategies for improved intravesical chemotherapy. The plant lectin wheat germ agglutinin (WGA) was immobilized on poly(lactide-co-glycolide) (PLGA) microparticles (MP) to induce stable cytoadhesion via cellular carbohydrate chains, similar to the specific attachment mechanism utilized by uropathogenic bacteria. A panel of DNA-selective chemotherapeutics with established track record in uro-oncology was screened for physicochemical compatibility with the polymeric carrier formulation. Critical limitations in encapsulation efficiency were found for mitomycin C (MMC), doxorubicin (DOX), and gemcitabine hydrochloride (GEM), despite multiparametric optimization of the preparation conditions. In contrast, the amphiphilic 4-(N)-stearoyl prodrug of gemcitabine (GEM-C18) exhibited excellent processability with PLGA. In vitro bioassays on 5637 human BCa cells showed that the enhanced cytoadhesion of WGA-GEM-C18-PGLA-MP traces back to the specific lectin/carbohydrate interaction, and is not easily disrupted by adverse environmental factors. Owing to several synergistic effects, the combined prodrug/targeting approach resulted in strong cytostatic response even when adjusting the exposure scheme to the confined temporal conditions of instillative treatment. Our results highlight the importance of fine-tuning both pharmacokinetic and pharmacologic parameters to gain adequate impact on urothelial cancer cells, and assign promising potential to glycan-targeted delivery concepts for the intravesical route.

[700]

TÍTULO / TITLE: Cytogenetic characterization of an N-butyl-N-(4-hydroxybutyl) nitrosamine-induced mouse papillary urothelial carcinoma.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Arantes-Rodrigues R; Pinto-Leite R; da Costa RG; Colaco A; Lopes C; Oliveira P

INSTITUCIÓN / INSTITUTION: Department of Veterinary Sciences, ECAV, University of Tras-os-Montes and Alto Douro, 5001-801, Vila Real, Portugal.

RESUMEN / SUMMARY: Chemically-induced urinary bladder cancer in rodents has long been used as a reliable model to study the biopathology of urinary bladder neoplasia and to develop therapeutic strategies against human tumors. Knowledge of the genetic basis underlying carcinogenesis would greatly enhance usability and usefulness of this model for the purposes of comparative pathology. However, little is known about the cytogenetic characteristics of rodent urinary bladder tumors. Accordingly, pathological and negative control specimens were collected for cytogenetic evaluation, from an ongoing mouse urinary bladder N-butyl-N-(4-hydroxybutyl) nitrosamine-induced carcinogenesis
study. Histopathological analysis characterized the pathological sample as a papillary urothelial carcinoma. Conventional cytogenetic analysis revealed the presence of 66.3% tetraploid cells. Fluorescent in situ hybridization using chromosome paint probes allowed the detection of a reciprocal translocation involving chromosomes 4 and 14 (containing the murine homologues to human p16 and retinoblastoma tumor-suppressor genes) in 42% of tetraploid cells. The control sample showed no histological or cytogenetic changes. CDKN2A and RB1 loss of heterozygosity is associated with human early and advanced urinary bladder cancer, respectively. Thus, the present data paves the way for further studies concerning the molecular mechanisms of urinary bladder carcinogenesis.

[701]

TÍTULO / TITLE: - Ultrasound improves the uptake and distribution of liposomal Doxorubicin in prostate cancer xenografts.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Eggen S; Afadzi M; Nilssen EA; Haugstad SB; Angelsen B; Davies Cde L
INSTITUCIÓN / INSTITUTION: - Department of Physics, Norwegian University of Science and Technology, Trondheim, Norway. Electronic address: siv.eggen@ntnu.no.
RESUMEN / SUMMARY: - Combining liposomally encapsulated cytotoxic drugs with ultrasound exposure has improved the therapeutic response to cancer in animal models; however, little is known about the underlying mechanisms. This study focused on investigating the effect of ultrasound exposures (1 MHz and 300 kHz) on the delivery and distribution of liposomal doxorubicin in mice with prostate cancer xenografts. The mice were exposed to ultrasound 24 h after liposome administration to study the effect on release of doxorubicin and its penetration through the extracellular matrix. Optical imaging methods were used to examine the effects at both microscopic subcellular and macroscopic tissue levels. Confocal laser scanning microscopy revealed that ultrasound-exposed tumors had increased levels of released doxorubicin compared with unexposed control tumors and that the distribution of liposomes and doxorubicin through the tumor tissue was improved. Whole-animal optical imaging revealed that liposomes were taken up by both abdominal organs and tumors.

[702]
Beclin 1 and its emerging role as a prognostic biomarker in systemic malignancies besides bladder carcinomas.


Kapoor S

Private practice, Mechanicsville, VA, USA.

Chemokines and chemokine receptors as promoters of prostate cancer growth and progression.


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Sheila and David Fuente Graduate Program in Cancer Biology, University of Miami School of Medicine, Miami, Florida, USA.

Prostate cancer (CaP) is estimated to be first in incidence among cancers, with more than 240,000 new cases in 2012 in the United States. Chemokines and their receptors provide survival, proliferation, and invasion characteristics to CaP cells in both primary sites of cancer and metastatic locations. The emerging data demonstrate that many chemokines and their receptors are involved in the multistep process of CaP, leading to metastasis, and, further, that these factors act cooperatively to enhance other mechanisms of tumor cell survival, growth, and metastasis. Changes of chemokine receptor cohorts may be necessary to activate tumor-promoting signals. Chemokine receptors can activate downstream effectors, such as mitogen-activated protein kinases, by complex mechanisms of ligand-dependent activation of cryptic growth factors; guanosine triphosphate-binding, protein-coupled activation of survival kinases; or transactivation of other receptors such as ErbB family members. We describe vanguard research in which more than the classic view of chemokine receptor biology was clarified. Control of chemokines and inhibition of their receptor activation may add critical tools to reduce tumor growth, especially in chemo-hormonal refractory CaP that is both currently incurable and the most aggressive form of the disease, accounting for most of the more than 28,000 annual deaths.


Enlace al Resumen / Link to its Summary

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Enlace al texto completo (gratuito o de pago)
RESUMEN / SUMMARY: - OBJECTIVE: El objetivo de este estudio fue evaluar la precisión de la TC multidetector en el diagnóstico de invasión de grasa perinefrática (PN) y/o renal (RS) en pacientes con carcinoma renal (RCC), con referencia a los hallazgos de la CT predictivos para el diagnóstico de invasión. 

MÉTODOS: Se realizó un estudio retrospectivo con 48 RCCs. Examinaciones se realizaron en un escáner de CT de 16 filas, incluyendo imágenes de TC no contrastadas y de 3 fases de contraste. Las imágenes transversales no contrastadas y las reformaciones multiplanares de cada fase de contraste-contrastado CT se evaluaron. La valúe predictiva de los hallazgos de CT en el diagnóstico de PN y/o RS grasa invasión fue determinada utilizando análisis de regresión logística multivariante. 

RESULTADOS: Los hallazgos de la CT que fueron más predictivos para el diagnóstico de PN grasa invasión fueron el nódulo contrastado en la grasa PN y alrededor de la masa tumoral. La invasión del sistema pelvicalyceal fue el predictor más significativo para el diagnóstico de RS grasa invasión. 

CONCLUSIONES: La TC multidetector proporciona resultados satisfactorios en el diagnóstico de PN y/o RS grasa invasión en RCC.
Dutasteride. Flavonoids such as silibinin, green tea polyphenols, genistein, curcumin have shown great promise, but avenues to improve their bioavailability are requisite. Agents with antioxidant potentials like lycopene, selenium, and vitamin E have also been explored. Antioxidant trials have yielded mixed results or benefitted only a subgroup of population, although further studies are needed to establish them as preventive agent. Although a majority of the trials resulted in positive outcomes supporting their role as preventive agents; one should be cautious of neutral or negative results as well. For clinical applicability of these agents, we need to identify the ideal target population, time of intervention, appropriate dosage, and extent of intervention required. Incoherency of data with these agents urges for a stringent study design and thorough interpretation to accurately judge the necessity and feasibility of the preventive measures.
beyond the stent segment (75.0%), followed by reactive hyperplasia at the stent tips (12.5%), bladder invasion of the primary tumor (8.0%), and stent-related pain (8.0%). Twelve patients had overall success after secondary Uventa™ placement. There were no severe complications. The complications included persistent flank pain (15.5%), lower urinary tract symptoms (7.0%), acute pyelonephritis (2.8%), stent migration (2.8%), and persistent hematuria (2.8%). Conclusions: These data show that UventaTM can be an effective and safe option for palliative treatment of MUO in a large series of patients.

[707]  
**TITULO / TITLE:** Peripelvic/periureteral fat invasion is independently associated with worse prognosis in pT3 upper tract urothelial carcinoma.  
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary  
**AUTORES / AUTHORS:** Park J; Park S; Song C; Hong JH; Kim CS; Ahn H  
**INSTITUCIÓN / INSTITUTION:** Department of Urology, Eulji University Hospital, Daejeon, Korea.  
**RESUMEN / SUMMARY:** PURPOSE: To elucidate the reasons for conflicting results regarding the prognostic significance of tumor location in upper tract urothelial carcinoma (UTUC), we analyzed the stage-specific impact of tumor location on oncological outcomes following radical nephroureterectomy (RNU). METHODS: Data from 392 patients who underwent RNU with curative intent between 1991 and 2010 were reviewed. Prognostic impact of tumor location and various clinicopathological factors for recurrence-free survival (RFS) and cancer-specific survival (CSS) was evaluated using Kaplan-Meier and Cox regression analyses at each pathological stage. Tumor location was classified as renal pelvis or ureter, and pT3 tumors were further stratified as invading the renal parenchyma or peripelvic or periureteral fat. RESULTS: In stage-specific analysis, tumor location did not have prognostic significance in patients with \(<\!/=\)pT2 tumors, whereas RFS and CSS rates were significantly lower in patients with pT3 ureteral tumors than renal pelvic tumors. Subgroup analysis showed that RFS and CSS rates were significantly higher for pT3 tumors invading the renal parenchyma than the peripelvic or periureteral fat. On multivariate analysis in pT3 tumors adjusting other clinicopathological parameters, tumor location remained significant predictors for both RFS and CSS. Compared with tumors invading renal parenchyma, tumors invading peripelvic fat or periureteral fat were associated with about 3.5 times higher risk for cancer-specific mortality (p < 0.05). CONCLUSIONS: Location-dependent survival difference exists only in patients with pT3 UTUC. Conflicting
in institutional results regarding tumor location in UTUC may be due to difference in the proportions of parenchymal versus peripelvic fat invasion in pT3 pelvic tumors.

[708]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ondrusova M; Mrozova L; Ondrus D; Mrinakova B
RESUMEN / SUMMARY: - Prostate cancer is the third most-common non-skin cancer and also the third leading cause of cancer death in the Slovak Republic in recent years. However, analysis of incidence and mortality long-term trends, on the basis of which the prevalence estimates could have been calculated, were not available. This paper analyses national trends in prostate cancer incidence and mortality from 1968 to 2007 by using the join-point regression to propose potential changes in health care. The authors noted a statistically significant increase in the values of incidence after 1999 and improvement in mortality after 1998. Using a mathematical modelation authors predicted the overall prostate cancer prevalence in the Slovak Republic to provide actual data for health management. Keywords: prostate cancer - epidemiology, incidence, mortality, prevalence.

[709]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES //authors: - Grigoryev A; Kavanagh P; Melnik A; Savchuk S; Simonov A
INSTITUCIÓN / INSTITUTION: - 1Bureau of Forensic-Medical Expertise’s, Forensic-Chemical Division, Belgorod, Russia.
RESUMEN / SUMMARY: - Studies on the pyrolysis of the synthetic cannabinoid agonist UR-144 ((1-pentyl-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone) have shown that its major pyrolysis product is a tetramethylcyclopropane ring-opened alkene. Considering that smoking is a common way of ingesting synthetic cannabinoids, the presence of the
metabolites of this pyrolysis product would be expected in biological fluids. Using GC-MS and LC-MS-MS methods, a series of phase I metabolites of UR-144 and its pyrolysis product were detected in the urine samples from patients admitted to hospital with suspected drug intoxication. The metabolites were tentatively identified as the products of mono-hydroxylation, di-hydroxylation, mono-hydroxylation with formation of the carbonyl group on the N-alkyl chain, carboxylation and N-dealkylation with mono-hydroxylation. In the case of the UR-144 pyrolysis product, metabolites with hydration of the aliphatic double bond were also identified. The parent compounds were detected as trace amounts in some urine samples, and the hydrated derivative of the UR-144 pyrolysis product was detected in the majority of samples. The detection of mono-hydroxylated metabolites of UR-144 (LC-MS-MS) and mono-hydroxylated/with hydration metabolites of the UR-144 pyrolysis product (GC-MS) was found to be the most useful method of establishing UR-144 ingestion.
INTRODUCTION: Standardized methods of reporting complications after radical cystectomy (RC) and urinary diversions (UD) are necessary to evaluate the morbidity associated with this operation to evaluate the modified Clavien classification system (CCS) in grading perioperative complications of RC and UD in a real life cohort of patients with bladder cancer.

MATERIALS AND METHODS: A consecutive series of patients treated with RC and UD from April 2011 to March 2012 at 19 centers in Italy was evaluated. Complications were recorded according to the modified CCS. Results were presented as complication rates per grade. Univariate and binary logistic regression analysis were used for statistical analysis.

RESULTS: Results and limitations: 467 patients were enrolled. Median age was 70 years (range 35-89). UD consisted in orthotopic neobladder in 112 patients, ileal conduit in 217 patients and cutaneous ureterostomy in 138 patients. 415 complications were observed in 302 patients and were classified as Clavien type I (109 patients) or II (220 patients); Clavien type IIIa (45 patients), IIIb (22 patients); IV (11 patients) and V (8 patients). Patients with cutaneous ureterostomy presented a lower rate (8%) of CCS type >/=IIIa (p = 0.03). A longer operative time was an independent risk factor of CCS >/=III (OR: 1.005; CI: 1.002-1.007 per minute; p = 0.0001).

CONCLUSIONS: In our study, RC is associated with a significant morbidity (65%) and a reduced mortality (1.7%) when compared to previous experiences. The modified CCS represents an easily applicable tool to classify the complications of RC and UD in a more objective and detailed way.
TÍTULO / TITLE: - Phase II trial of first-line chemotherapy with gemcitabine, etoposide, and cisplatin for patients with advanced urothelial carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Urakami S; Fujii Y; Yamamoto S; Yuasa T; Kitsukawa S; Sakura M; Yano A; Saito K; Masuda H; Yonese J; Fukui I

INSTITUCIÓN / INSTITUTION: - Department of Urology, Cancer Institute Hospital, Japanese Foundation of Cancer Research, Tokyo, Japan. Electronic address: shinji.urakami@jfcr.or.jp.

RESUMEN / SUMMARY: - OBJECTIVES: This study sought to examine the combination chemotherapy of gemcitabine, etoposide, and cisplatin (GEP) as a first-line treatment for advanced urothelial carcinoma (UC) to assess its antitumor activity and toxicity. METHODS AND MATERIALS: Eligible patients with advanced UC had undergone no previous chemotherapy. Advanced UC was defined as unresectable or metastatic disease. Subsequent recurrent disease, either locally or distantly following primary radical surgery, was not excluded. GEP was recycled every 4 weeks. Etoposide and cisplatin were given on days 1 through 3 at doses of 60mg/m2 and 20mg/m2, respectively, and gemcitabine was given on days 1, 8, and 15 at a dose of 800mg/m2. The primary end point was objective response rate, and the secondary end points included progression-free survival, overall survival (OS), and toxicity. RESULTS: Forty-two patients were enrolled and subsequently treated with GEP. Nineteen had visceral/bone metastases, 16 had disease restricted to the lymph nodes, and the remaining 7 had unresectable disease at the primary site. The median number of GEP courses was 4. Thirty of the 42 assessable patients (71.4%, 95% confidence interval [CI]: 56.4%-82.8%) demonstrated objective responses. At a median follow-up of 14.6 months, median progression-free survival and OS periods were 8.7 months (95% CI: 6.9-14.6mo) and 16.2 months (95% CI: 13.1-25.4mo), respectively. In the multivariate analysis, anemia and visceral/bone metastasis were significant pretreatment prognostic factors for OS. Grade 4 hematologic events were neutropenia (83.3%), thrombocytopenia (23.8%), and anemia (7.1%). There were no toxic deaths and no instances of severe nonhematologic toxicity. CONCLUSIONS: GEP as a first-line chemotherapy treatment was very active and moderately tolerable for advanced UC. Anemia and visceral/bone metastasis were important negative predictive factors of GEP for OS.

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[713]
TÍTULO / TITLE: A bioengineered microenvironment to quantitatively measure the tumorigenic properties of cancer-associated fibroblasts in human prostate cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Clark AK; Taubenberger AV; Taylor RA; Niranjan B; Chea ZY; Zotenko E; Sieh S; Pedersen JS; Norden S; Frydenberg M; Grummet JP; Pook DW; Stirzaker C; Clark SJ; Lawrence MG; Ellem SJ; Hutmacher DW; Risbridger GP

INSTITUCIÓN / INSTITUTION: Department of Anatomy and Developmental Biology, School of Biomedical Sciences, Monash University, Clayton, Melbourne, Vic 3800, Australia.

TÍTULO / TITLE: Non-muscle invasive bladder cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Clark AK; Taubenberger AV; Taylor RA; Niranjan B; Chea ZY; Zotenko E; Sieh S; Pedersen JS; Norden S; Frydenberg M; Grummet JP; Pook DW; Stirzaker C; Clark SJ; Lawrence MG; Ellem SJ; Hutmacher DW; Risbridger GP

INSTITUCIÓN / INSTITUTION: Department of Anatomy and Developmental Biology, School of Biomedical Sciences, Monash University, Clayton, Melbourne, Vic 3800, Australia.
TÍTULO / TITLE: - uPA/PAI-1 ratios distinguish benign prostatic hyperplasia and prostate cancer.
RESUMEN / SUMMARY: - PURPOSE: Urokinase plasminogen activator (uPA) and its inhibitor type 1 (PAI-1) are associated with tumour metabolism and are widely considered to be informative for the identification of cancer. We have analysed prostate tissue resections from patients with prostate cancer (PCa) and with benign prostatic hyperplasia (BPH) for protein levels of uPA and PAI-1, and searched for distinctions between these two clinical manifestations.
METHODS: Prostate tissue was deep frozen in liquid N2 and homogenized in a stainless steel punch homogenizer. The tissue powder was extracted with a pH 8.5 TRIS/Triton X-100 buffer, and the extract analysed by FEMTELLE assay to generate uPA and PAI-1 readings in ng/mg protein. The uPA/PAI-1 ratio was calculated for each sample, and the mean ratios for the two diagnostic groups were compared. RESULTS: The concentration of uPA (mean +/- SD) was found to be 0.19 +/- 0.04 ng/mg protein (range 0.05-0.72 ng/mg) and 0.15 +/- 0.02 ng/mg protein (range 0.03-0.78 ng/mg) in PCa and BPH samples, respectively. The concentration of PAI-1 was found to be 4.93 +/- 0.90 ng/mg (range 1.10-11.80 ng/mg) and 5.87 +/- 0.70 ng/mg (range 0.2-25.0 ng/mg) in PCa and BPH samples, respectively. A consistent finding being that PAI-1 concentrations exceed uPA concentrations by far giving rise to characteristic uPA/PAI-1 ratios. In BPH samples, there was a trend of PAI-1 to increase with uPA content, while in PCa samples, PAI-1 remained fairly constant. The mean uPA/PAI-1 ratio in PCa samples was found to be 0.06 +/- 0.01 and was significantly higher than in BPH samples where the mean uPA/PAI-1 ratio was 0.03 +/- 0.003 (p = 0.0028). R^2 = 0.1389. CONCLUSION: Using a contingent of 62 patients of which 46 were BPH and 16 were PCa, we report definitive concentrations of uPA and PAI-1 in tumour tissue extracts and show that the
uPA/PAI-1 ratio emerges as a candidate marker to distinguish between BPH and PCa.

[716]
**TÍTULO / TITLE:** Apparent diffusion coefficient value reflects invasive and proliferative potential of bladder cancer.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** Kobayashi S; Koga F; Kajino K; Yoshita S; Ishii C; Tanaka H; Saito K; Masuda H; Fujii Y; Yamada T; Kihara K
**INSTITUCIÓN / INSTITUTION:** Department of Urology, Tokyo Medical and Dental University Graduate School, Tokyo, Japan.
**RESUMEN / SUMMARY:** PURPOSE: To elucidate a role of apparent diffusion coefficient (ADC) value as a biomarker of bladder cancer, we investigated its associations with Ki-67 labeling index (LI) along with classical clinicopathological prognosticators. MATERIALS AND METHODS: Diffusion-weighted MRI (DW-MRI) at 1.5 Tesla using b-values of 0, 500, 1000, and 2000 s/mm2 was prospectively taken before transurethral resection by 132 bladder cancer patients. ADC value of index tumors was measured and compared with clinicopathological prognosticators including Ki-67 LI. RESULTS: ADC value was significantly lower in tumors with higher Ki-67 LIs, sessile tumors (versus papillary), larger tumors, higher grade disease, and higher T stage disease. ADC value inversely correlated with Ki-67 LI (rho = -0.57; P < 0.0001). On multiple regression analysis, T stage and Ki-67 LI significantly correlated with ADC value. The Akaike information criterion confirms these two parameters constitute the best model for determining ADC value. Similarly, T stage and ADC value significantly correlated with Ki-67 LI and these two parameters composed the best model for predicting Ki-67 LI. CONCLUSION: ADC value would reflect T stage and Ki-67 LI, representing invasive and proliferative potential, respectively. ADC value is likely to serve as a biomarker reflecting aggressiveness of bladder cancer. J. Magn. Reson. Imaging 2013. © 2013 Wiley Periodicals, Inc.

[717]
**TÍTULO / TITLE:** Molecular characteristics of malignant ovarian germ cell tumors and comparison with testicular counterparts: implications for pathogenesis.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
This review focuses on the molecular characteristics and development of rare malignant ovarian germ cell tumors (mOGCTs). We provide an overview of the genomic aberrations assessed by ploidy, cytogenetic banding, and comparative genomic hybridization. We summarize and discuss the transcriptome profiles of mRNA and microRNA (miRNA), and biomarkers (DNA methylation, gene mutation, individual protein expression) for each mOGCT histological subtype. Parallels between the origin of mOGCT and their male counterpart testicular GCT (TGCT) are discussed from the perspective of germ cell development, endocrinological influences, and pathogenesis, as is the GCT origin in patients with disorders of sex development. Integrated molecular profiles of the 3 main histological subtypes, dysgerminoma (DG), yolk sac tumor (YST), and immature teratoma (IT), are presented. DGs show genomic aberrations comparable to TGCT. In contrast, the genome profiles of YST and IT are different both from each other and from DG/TGCT. Differences between DG and YST are underlined by their miRNA/mRNA expression patterns, suggesting preferential involvement of the WNT/beta-catenin and TGF-beta/bone morphogenetic protein signaling pathways among YSTs. Characteristic protein expression patterns are observed in DG, YST and IT. We propose that mOGCT develop through different developmental pathways, including one that is likely shared with TGCT and involves insufficient sexual differentiation of the germ cell niche. The molecular features of the mOGCTs underline their similarity to pluripotent precursor cells (primordial germ cells, PGCs) and other stem cells. This similarity combined with the process of ovary development, explain why mOGCTs present so early in life, and with greater histological complexity, than most somatic solid tumors.
AUTORES / AUTHORS: - Padrao AI; Oliveira P; Vitorino R; Colaco B; Pires MJ; Marquez M; Castellanos E; Neuparth MJ; Teixeira C; Costa C; Moreira-Goncalves D; Cabral S; Duarte JA; Santos LL; Amado F; Ferreira R

INSTITUCIÓN / INSTITUTION: - QOPNA, Chemistry Department, University of Aveiro, Aveiro, Portugal.

RESUMEN / SUMMARY: - Loss of skeletal muscle is a serious consequence of cancer as it leads to weakness and increased risk of death. To better understand the interplay between urothelial carcinoma and skeletal muscle wasting, cancer-induced catabolic profile and its relationship with muscle mitochondria dynamics were evaluated using a rat model of chemically induced urothelial carcinogenesis by the administration of N-butyl-N-(4-hydroxybutyl)-nitrosamine (BBN). The histologic signs of non-muscle-invasive bladder tumors observed in BBN animals were related to 17% loss of body weight and high serum levels of IL-1beta, TNF-alpha, TWEAK, C-reactive protein, myostatin and lactate and high urinary MMPs activities, suggesting a catabolic phenotype underlying urothelial carcinoma. The 12% loss of gastrocnemius mass was related to mitochondrial dysfunction, manifested by decreased activity of respiratory chain complexes due to, at least partially, the impairment of protein quality control (PQC) systems involving the mitochondrial proteases paraplegin and Lon. This was paralleled by the accumulation of oxidatively modified mitochondrial proteins. In overall, our data emphasize the relevance of studying the regulation of PQC systems in cancer cachexia aiming to identify therapeutic targets to counteract muscle wasting.

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TÍTULO / TITLE: - A cost-minimisation analysis comparing photoselective vaporisation (PVP) and transurethral resection of the prostate (TURP) for the management of symptomatic benign prostatic hyperplasia (BPH) in Queensland, Australia.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Whitty JA; Crosland P; Hewson K; Narula R; Nathan TR; Campbell PA; Keller A; Scuffham PA

INSTITUCIÓN / INSTITUTION: - Centre for Applied Health Economics, School of Medicine, and Population and Social Health Research Program, Griffith Health Institute, Griffith University, Meadowbrook.

RESUMEN / SUMMARY: - OBJECTIVES: To compare the costs of photoselective vaporisation (PVP) and transurethral resection of the prostate (TURP) for management of symptomatic benign prostatic hyperplasia (BPH) from the perspective of a Queensland public hospital provider. PATIENTS AND METHODS: A decision-analytic model was used to compare the costs of PVP...
and TURP. Cost inputs were sourced from an audit of patients undergoing PVP or TURP across three hospitals. The probability of re-intervention was obtained from secondary literature sources. Probabilistic and multi-way sensitivity analyses were used to account for uncertainty and test the impact of varying key assumptions. RESULTS: In the base case analysis, which included equipment, training and re-intervention costs, PVP was AU$ 739 (95% credible interval [CrI] -12 187 to 14 516) more costly per patient than TURP. The estimate was most sensitive to changes in procedural costs, fibre costs and the probability of re-intervention. Sensitivity analyses based on data from the most favourable site or excluding equipment and training costs reduced the point estimate to favour PVP (incremental cost AU$ -684, 95% CrI -8319 to 5796 and AU$ -100, 95% CrI -13 026 to 13 678, respectively). However, CrIs were wide for all analyses. CONCLUSIONS: In this cost minimisation analysis, there was no significant cost difference between PVP and TURP, after accounting for equipment, training and re-intervention costs. However, PVP was associated with a shorter length of stay and lower procedural costs during audit, indicating PVP potentially provides comparatively good value for money once the technology is established.

[720]

RESUMEN / SUMMARY: - Bladder adenocarcinoma 41 years after augmentation enterocystoplasty for tuberculosis].

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Quinta A; Carvalho AP; Oliveira M; Oliveira C; Ribeiro Santos A

INSTITUCIÓN / INSTITUTION: - Urology Department, Hospital Sao Marcos, Braga, Portugal. andremquinta@gmail.com

RESUMEN / SUMMARY: - OBJECTIVE: To report a case of adenocarcinoma arising in an augmented bladder 41 years after the procedure. METHODS: After troublesome evaluation and fistula closure with urinary diversion by percutaneous nephrostomy, the patient underwent palliative chemotherapy and radiotherapy. RESULT: He died 5 months after the onset of the fistula. CONCLUSIONS: Development of adenocarcinoma in augmentation enterocystoplasties implies a mortality of about 30%. Early detection requires a high index of suspicion. Surveillance of augmented bladders, by annual cystoscopy and urine cytology, is therefore recommended.

[721]

CASTELLANO -
Carcinoma basaloide de la próstata: un tumor extremadamente raro.

Basaloid carcinoma of the prostate: an extremely rare tumor.

**RESUMEN / SUMMARY:**
Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:**

**AUTORES / AUTHORS:**
Rodríguez-Carlin A; Arellano L; Lopez-Fontana G; Bolufer E; Castillo OA

**INSTITUCIÓN / INSTITUTION:**
Urology Department. Clinica Indisa. Facultad de Medicina. Universidad Andres Bello. Chile.

**RESUMEN / SUMMARY:**
OBJECTIVE: The basaloid carcinoma of the prostate (BC) is a rare malignant neoplasm arising from the basal cells of prostatic ducts and acini. We report a case and review the literature.

METHODS: A 76-year-old man presented with symptoms of lower obstructive uropathy, the IPSS score was 29 and prostate specific antigen (PSA) of 0.924 ng/ml. Transurethral resection of prostate (TURP) was performed in September 2008, histopathological diagnosis was BC. In February 2009 laparoscopic radical prostatectomy was performed.

RESULTS: Histopathological examination revealed a BC with adenoid cystic growth pattern, perineural infiltration and focal involvement of the left seminal vesicle. Immunohistochemically, the cells were negative for PSA, stained and were strongly positive for specific monoclonal antibodies anti-cytokeratin 34betaE12, p63 and BCL2. The patient has 23 months of follow-up, with complete continence and no evidence of tumor recurrence.

CONCLUSIONS: The BC is an extremely rare subtype of malignant tumors of the prostate, where immunohistochemistry plays a fundamental role in diagnosis.

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Clinical debut of a prostatic cancer with metastasis in manubrium sterni.

**RESUMEN / SUMMARY:**
Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:**

**AUTORES / AUTHORS:**
Rodriguez Collar TL; Matos Quesada D; Baez Sarria F

**INSTITUCIÓN / INSTITUTION:**
Servicio de Urología y Medicina Interna, Hospital Unviersitario Dr. Carlos J. Finlay, La Habana, Cuba. hidalgo@erkasl.co.cu

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Cutaneous metastasis from renal clear cell carcinoma.

**RESUMEN / SUMMARY:**
Enlace al Resumen / Link to its Summary

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538
Metastatic colon carcinoma to the prostate gland.

We present a case report of a 70-year-old man with a known history of sigmoid adenocarcinoma, treated with chemotherapy and surgical resection of synchronous lung metastases. Four years after initial diagnosis, the patient was diagnosed with metastases to the prostate gland, proven pathologically. To our knowledge, colon adenocarcinoma metastasizing to the prostate has not been previously described on magnetic resonance imaging and positron emission tomography-computed tomography.

Adrenomedullin (ADM) is a potent, long-lasting angiogenic peptide that was originally isolated from human pheochromocytoma. ADM signaling is of particular significance in endothelial cell biology because the peptide protects cells from apoptosis, and ADM has been shown to be pro-tumorigenic in that it stimulates tumor cell growth and angiogenesis. ADM may
be involved in micro-vessel proliferation and partially in the release of hypoxia in solid tumors, contributing to the proliferation of tumor cells as well as local tumor invasion and metastasis. However, the effect of hypoxia-induced ADM expression in bladder cancer remains unclear. Here, we found that the levels of ADM protein in tumor tissue from patients with bladder urothelial cell carcinoma were significantly increased compared to the adjacent non-tumor bladder tissues (p < 0.01). Under hypoxic conditions, the expression of ADM was significantly elevated in a time-dependent manner in human bladder cancer cell lines. Furthermore, the knockdown of ADM by shRNA in T24 cells showed obvious apoptosis compared to untransfected controls (p < 0.0001). In addition, the combination of cisplatin and ADM-shRNA significantly reduces the tumor growth in vivo compared to treatment with cisplatin (p = 0.0046) or ADM-shRNA alone (p < 0.0001). These data suggest that ADM plays an important role in promoting bladder cancer cell growth under hypoxia and that the inhibition of ADM may provide a target for bladder cancer therapy.

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RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Borovskaya TG; Fomina TI; Ermolaeva LA; Vychuzhanina AV; Pakhomova AV; Poluektova ME; Shchemerova YA
INSTITUCIÓN / INSTITUTION: - Institute of Pharmacology, Siberian Division of the Russian Academy of Medical Sciences, Tomsk, Russia.
repropharm@yandex.ru.
RESUMEN / SUMMARY: - Comparative evaluation of the efficiency of prostatotropic agents was carried out in rat experiments. Serenoa repens plant preparation and polypeptides isolated from the cattle prostate were used for the treatment of benign hyperplasia. Drugs in parallel with sulpiride similarly led to shrinkage of the acinar epithelial area and to emergence of a trend to an increase of the stromal/epithelial proportion, more so after Serenoa repens treatment.

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RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

540
Paraneoplastic syndromes may affect the central and peripheral nervous system of adults and children with cancer. Neurological symptoms may resolve with treatment of the underlying neoplasm. We report the case of a child with Wilms tumor who presented with generalized weakness, fatigue, ptosis, hypokinesis, dysarthria, urinary retention, facial diplegia, ophthalmoplegia, and autonomic dysfunction. Routine electrodiagnostic testing, including repetitive nerve stimulation, was normal. Clinical features and stimulation single-fiber electromyogram were consistent with a neuromuscular junction transmission disorder, likely Lambert-Eaton myasthenic syndrome. The child’s neurological status returned to normal with successful treatment of the tumor.
cytokeratin 7 (CK7) immunostaining were performed. Genomic profile was established by array comparative genomic hybridisation (array-CGH) on frozen samples. Mean age at diagnosis was 70 years (range 46-83). No recurrence was observed (median follow-up: 18 months; range 9-72). Tumour size ranged from 1 to 11 cm. HOCT showed an admixture of RO- and ChRCC-like areas and/or “hybrid” cells with overlapping cytonuclear and/or histochemical features. Hale staining was apical in 50 to 100 % of cells, and CK7 was expressed in 10 to 100 % of cells. Genomic profile was balanced in seven cases or showed a limited number of random imbalances in five cases, as observed in RO. In no instances were observed the characteristic chromosome losses of ChRCC. These results suggest that so called HOCT are not true hybrid tumours and rather could represent a morphological variant of RO. From a diagnostic perspective, an array-CGH analysis could be performed in ambiguous ChRCC/RO cases to formally exclude the diagnosis of ChRCC.

[729]

**TITULO / TITLE:** - Prognostic utility of quantitative image analysis of microvascular density in prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Pathol Int. 2013 May;63(5):277-82. doi: 10.1111/pin.12056.

**AUTORES / AUTHORS:** - Ozerdem U; Wojcik EM; Duan X; Ersahin C; Barkan GA

**INSTITUCIÓN / INSTITUTION:** - Department of Pathology, Loyola University Medical Center, Chicago, Illinois, USA.

**RESUMEN / SUMMARY:** - The walls of angiogenic blood vessel capillaries are composed of two principal cell types, blood vessel endothelial cells (BEC) and pericytes (PC), whereas the walls of lymphatic capillaries are composed of lymphatic endothelial cells (LEC). In this investigation we describe a practical application of NIH ImageJ software for quantitative image analysis for pericytes and endothelial cells in prostate cancer. We used a tissue microarray that contained 49 tissue cores (normal prostate tissue or prostatic carcinomas with Gleason scores of 6 through 10). These prostate cancer samples represented AJCC prognostic stages II, III, and IV. Slides were immunostained with anti-PDGFR-beta antibody for identification of PC, and quantified as microvascular pericyte density (MVPD); they were also immunostained with anti-CD34 antibody for identification of LEC and BEC simultaneously, and quantified as microvascular endothelial density (MVED). CD31 and D2-40 immunostains were used to quantify BEC and lymphatic endothelial cells, respectively. Our results showed higher MVPD and MVED in prostate cancers with higher Gleason scores and higher stages, suggesting the prognostic utility of vascular image analysis in prostate pathology. This investigation demonstrates the
feasibility, versatility, and ease of use of ImageJ software and pericyte-specific and endothelial-specific immunohistochemistry for quantitative image analysis in prostate pathology.

[730] TÍTULO / TITLE: - Advocacy for Renal Biopsy Based on Two Cases of Mixed Epithelial and Stromal Tumour.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

Enlace al texto completo (gratuito o de pago) 1159/000348749

AUTORES / AUTHORS: - Ingels A; Verine J; Belle Mbou V; Desgrandchamps F; Tariel E; Mongiat-Artus P; Ploussard G
INSTITUCIÓN / INSTITUTION: - Departments of Urology and Pathology, CHU Saint-Louis, APHP, Paris, France.
RESUMEN / SUMMARY: - We report 2 cases of mixed epithelial and stromal tumours revealed by flank pain in a 56-year-old woman and by a renal biopsy in another asymptomatic woman. A greater awareness among urologists and radiologists of the features of mixed epithelial and stromal tumours could help evoke this diagnosis preoperatively leading to needle biopsy and to the most appropriate type of renal surgery.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

Enlace al texto completo (gratuito o de pago) 1016/j.toxlet.2013.04.021

AUTORES / AUTHORS: - Li JR; Cheng CL; Yang CR; Ou YC; Wu MJ; Ko JL
INSTITUCIÓN / INSTITUTION: - Institute of Medicine, Chung Shan Medical University, Taiwan; Division of Urology, Department of Surgery, Taichung Veterans General Hospital, Taiwan; Institute of Medical and Molecular Toxicology, Chung Shan Medical University, Taiwan.
RESUMEN / SUMMARY: - PURPOSE: Therapeutically induced autophagic cell death has been proven to be effective in cases of solid tumors. The dual phosphatidylinositol 3-kinase (PI3K) and mammalian target of rapamycin (mTOR) inhibitor NVP-BEZ235 possesses antitumor activity against solid tumors. Inhibition of mTOR has been shown to elicit autophagy. In this study, we examined the antiproliferation and autophagic activities of NVP-BEZ235 in
parental and cisplatin-resistant urothelial carcinoma (UC) cells. MATERIALS AND METHODS: Two UC cell lines, NTUB1 and a cisplatin-resistant subline N/P(14), were applied to examine the cytotoxic effect of NVP-BEZ235. The cell death mechanism was also evaluated. RESULTS: NVP-BEZ235 was effective in inhibiting the growth of UC cells including parental and cisplatin-resistant cells on flow cytometry assay and Western blot. Although NVP-BEZ235 did not induce LC3-II conversion, it did elicit acidic vesicular organelle (AVO) development on flow cytometry. On Western blot, NVP-BEZ235 decreased p62 and phospho-Rb expressions in a concentration-dependent manner. GFP-LC3 conversion and the appearance of cleaved-GFP following NVP-BEZ235 treatment were demonstrated on Western blot. In addition, lysosomotropic inhibition of autophagy by chloroquine (CQ), an agent that is currently in clinical use and a known antagonist of autophagy, resulted in proliferation of UC cells. Thus, inhibition of autophagic flux by CQ appears to be a survival mechanism that counteracts the anticancer effects of NVP-BEZ235. CONCLUSIONS: We demonstrated that NVP-BEZ235 inhibits UC cell proliferation by activating autophagic flux and cell cycle arrest, but does not induce apoptotic cell death. Our findings suggest that the anticancer efficacy of NVP-BEZ235 is due to autophagic flux and co-treatment with CQ counteracts the cytotoxic effect.

[732]

TÍTULO / TITLE: - Semen quality and associated reproductive indicators in middle-aged males: the role of non-malignant prostate conditions and genital tract inflammation.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ausmees K; Korrovits P; Timberg G; Punab M; Mandar R

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Tartu University, Tartu, Estonia.

RESUMEN / SUMMARY: - PURPOSE: To compare the associations between non-malignant prostate conditions, genital tract inflammation, and reproductive function in middle-aged men. METHODS: Three-hundred and eighty-two voluntary male subjects who underwent the screening for prostate health were recruited for the study. Semen quality and associated reproductive indicators, seminal inflammation, and prostate-related pathologies were evaluated. RESULTS: Sperm motility and prostate-related parameters were significantly impaired in patients with chronic prostatitis syndromes and lower urinary tract symptoms in comparison with controls. Elevated seminal markers of inflammation were in positive association with body mass index, prostate-
specific antigen, and estradiol level in serum while in negative association with semen volume, total sperm count, and sperm motility. According to WHO reference limits, speculative cutoff values for WBC and IL-6 in semen to detect reduced sperm parameters were 0.342 M/mL and 56.8 ng/L, respectively. CONCLUSIONS: According to our data, one of the possible pathways for impaired reproductive quality in male subjects >45 years could be related to infection and inflammation in the genital tract with subsequent (partial) obstruction and damage of prostate and other male accessory glands.

[733]
TÍTULO / TITLE: - How far is the horizon? From current targets to future drugs in advanced renal cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1007/s00345-013-1096-1
AUTORES / AUTHORS: - Kruck S; Merseburger AS; Stenzl A; Bedke J
INSTITUCIÓN / INSTITUTION: - Department of Urology, Eberhard-Karls-University Tuebingen, Hoppe-Seyler Strasse 3, 72076, Tuebingen, Germany, Stephan.Kruck@med.uni-tuebingen.de.
RESUMEN / SUMMARY: - PURPOSE: The proliferative control of renal cell cancer (RCC) via vascular endothelial growth factor and mammalian target of rapamycin inhibition by targeted agents has substantially improved survival rates for RCC patients with metastatic (m) disease. However, the management of mRCC remains challenging because some patients are primarily refractory to the approved targeted agents and most therapies eventually fail because of the development of an intractable drug resistance. Tumor progression is closely related to a persistent or restored proliferation via direct and indirect oncogenic signals. Although the elucidation of cancer cell proliferation in the “omics era" has revealed an enormous number of new potential targets, a comprehensive overview of the different pathways that might serve as new drug targets has become increasingly complex. METHODS/RESULTS: This review highlights the well-trodden pathways in mRCC that are inhibited by targeting agents and describes innovative modes of action within these pathways that are currently not targeted but are under exploration in clinical studies. Additionally, this paper highlights as future drug targets the components of tumor metabolism that supply the tumor cells with nutrition. CONCLUSIONS: These fundamental insights into RCC proliferation as a key driver of progression are urgently needed to overcome the currently improved but still limited targeted drug success.

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TÍTULO / TITLE: - Gleason score 7 adenocarcinoma of the prostate with lymph node metastases: analysis of 184 radical prostatectomy specimens.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Kryvenko ON; Gupta NS; Virani N; Schultz D; Gomez J; Amin A; Lane Z; Epstein JI

INSTITUCIÓN / INSTITUTION: - From the Department of Pathology, Henry Ford Hospital, Detroit, Michigan (Drs Kryvenko, Gupta, Schultz, Gomez, and Lane); the Department of Pathology, University of Michigan, Ann Arbor, Michigan (Dr Virani); the Department of Pathology, Rhode Island Hospital, Providence (Dr Amin); and the Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, Maryland (Dr Epstein).

RESUMEN / SUMMARY: - Context.-Prostate cancer (PC) with lymph node metastases (LN(+)) is relatively rare, whereas it is relatively common in disease with a Gleason score (GS) 8 to 10 and virtually never seen in PC with GS 6 or less. It is most variable in GS 7 PC. Objective.-To determine clinicopathologic features associated with GS 7 PC with LN(+) compared with a control group without lymph node metastases (LN(-)). Design.-We analyzed 184 GS 7 radical prostatectomies with LN(+) and the same number of LN(-) Gleason-matched controls. The LN(+) cases were GS 3 + 4 = 7 (n = 64; 34.8%), GS 4 + 3 = 7 (n = 66; 35.9%), GS 3 + 4 = 7 with tertiary 5 (n = 10; 5.4%), and GS 4 + 3 = 7 with tertiary 5 (n = 44; 23.9%). Results.-The LN(+) cases demonstrated higher average values in preoperative prostate-specific antigen (12.2 versus 8.1 ng/mL), percentage of positive biopsy cores (59.1% versus 42.9%), prostate weight (54.4 versus 49.4 g), number of LNs submitted (12.7 versus 9.4), incidence of nonfocal extraprostatic extension (82.6% versus 63.6%), tumor volume (28.9% versus 14.8%), frequency of lymphovascular invasion (78.3% versus 38.6%), intraductal spread of carcinoma (42.4% versus 20.7%), incidence of satellite tumor foci (16.4% versus 4.3%), incidence of pT3b disease (49.5% versus 14.7%), and lymphovascular invasion in the seminal vesicles (52% versus 30%). There were differences in GS 4 patterns and cytology between LN(+) and LN(-) cases, with the former having higher volumes of cribriform and poorly formed patterns, larger nuclei and nucleoli, and more-frequent macronucleoli. All P </= .05. Conclusion.-Gleason score 7 PC with LN(+) has features highlighting a more-aggressive phenotype. These features can be assessed as prognostic markers in GS 7 disease on biopsy (eg, GS 4 pattern, intraductal spread, cytology) or at radical prostatectomies (all variables), even in men without LN dissection or LN(-) disease.
TÍTULO / TITLE: - Nonneoplastic renal cortical scarring at tumor nephrectomy predicts decline in kidney function.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Salvatore SP; Cha EK; Rosoff JS; Seshan SV

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, New York 10065, USA.

CONTEXT: Evaluating nontumor portions of tumor nephrectomies is useful to diagnose nonneoplastic renal disease. OBJECTIVE: To determine the medical renal disease frequency and to assess the prognostic significance of the various renal pathologic variables with long-term follow-up in tumor nephrectomy patients. DESIGN: We reviewed nonneoplastic kidney sections of 456 consecutive cases from 1998 to 2008. Seventy-five cases were excluded (19 tumor compression, 25 no nonneoplastic tissue, 22 embolized kidneys, 9 end stage). Special staining, immunofluorescence, and/or electron microscopy was performed where appropriate. Vascular sclerosis was scored from mild to severe; interstitial fibrosis/tubular atrophy and global glomerulosclerosis (GS) were expressed as percentages. Follow-up, minimum 12 months, was evaluated in 156 cases. All renal pathologic variables were compared with regard to change in creatinine level from preoperative assessment to follow-up. RESULTS: Of 381 cases, 57 had additional medical renal disease (15%), most frequently diabetic nephropathy (28) and hypertensive nephropathy (11). Postoperative creatinine levels increased significantly in patients with severe arteriosclerosis or arteriolosclerosis, >5% GS, and >10% interstitial fibrosis/tubular atrophy. Seventy-four percent of cases with additional nonneoplastic diagnoses showed severe arteriolosclerosis. Higher corresponding GS was seen in the more affected vascular cases: mean, 5.56% GS for mild versus 23% GS for severe. Three patients progressed to renal failure 1 to 4 years after nephrectomy, 2 with hypertensive nephrosclerosis and 1 with diabetic nephropathy. CONCLUSIONS: Medical renal disease was identified in 15% of tumor nephrectomy specimens. The degrees of vascular sclerosis, GS, and interstitial fibrosis/tubular atrophy are predictive of elevated creatinine levels in postnephrectomy patients. Prognostic implications of the nontumor pathology are important in nephrectomized patients.
TÍTULO / TITLE: - Renal Lymph Nodes for Tumor Staging: Appraisal of 871 Nephrectomies With Examination of Hilar Fat.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Mehta V; Mudaliar K; Ghai R; Quek ML; Milner J; Flanigan RC; Picken MM

INSTITUCIÓN / INSTITUTION: - From the Departments of Pathology (Drs Mehta, Mudaliar, and Picken) and Urology (Drs Quek, Milner, and Flanigan), Loyola University Medical Center, Maywood, Illinois; and the Department of Pathology, Rush University Medical Center, Chicago, Illinois (Dr Ghai).

RESUMEN / SUMMARY: - Context.-Despite decades of research, the role of lymphadenectomy in the management of renal cell carcinoma (RCC) is still not clearly defined. Before the implementation of targeted therapies, lymph node metastases were considered to be a portent of markedly decreased survival, regardless of the tumor stage. However, the role of lymphadenectomy and the relative benefit of retroperitoneal lymph node dissection in the context of modern adjunctive therapies have not been conclusively addressed in the clinical literature. The current pathologic literature does not offer clear recommendations with regard to the minimum number of lymph nodes that should be examined in order to accurately stage the pN in renal cell carcinoma. Although gross examination of the hilar fat to assess the nodal status is performed routinely, it has not yet been determined whether this approach is adequate. Objective.-To evaluate the status of lymph nodes and their rate of identification in the pathologic examination of nephrectomy specimens in adult renal malignancies. Design.-We reviewed the operative and pathology reports of 871 patients with renal malignancies treated by nephrectomy. All tumors were classified according to the seventh edition of the Tumor-Node-Metastasis classification. Patients were divided into 3 groups: Nx, no lymph nodes recovered; N0, negative; and N1, with positive lymph nodes. Grossly visible lymph nodes were submitted separately; as per grossing protocol, hilar fatty tissue was submitted for microscopic examination. We evaluated the factors that affected the number of lymph nodes identified and the variables that allowed the prediction of nodal involvement. Results.-Lymph nodes were recovered in 333 of 871 patients (38%): hilar in 125 patients, nonhilar in 137 patients, and hilar and nonhilar in 71 patients. Patients with positive lymph nodes (n = 87) were younger, had larger primary tumors, and had lymph nodes of average size, as well as a higher pT stage, nuclear grade, and rate of metastases. Metastases were seen only in grossly identified lymph nodes (65% hilar, 16% nonhilar); all microscopic nodes were negative. Even with the microscopic examination of fat, hilar lymph nodes were recovered in only 22.5% of patients. A nonhilar route of node metastasis was suspected in 40 patients.
Conclusions.-Only grossly identifiable lymph nodes, both hilar and nonhilar, were positive for metastases. Although microscopic examination of the hilar fat increased the number of lymph nodes recovered, the identification rate of these nodes was low (22.5%), and such microscopic nodes were invariably negative. Hence, microscopic examination of the hilar fat may be unnecessary.

[737]

TÍTULO / TITLE: - Second to fourth digit ratio, handedness and testicular germ cell tumors.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Trabert B; Graubard BI; Erickson RL; Zhang Y; McGlynn KA

INSTITUCIÓN / INSTITUTION: - Hormonal and Reproductive Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Rockville, MD, USA. Electronic address: trabertbl@mail.nih.gov.

RESUMEN / SUMMARY: - BACKGROUND: Research on early life exposures and testicular germ cell tumors (TGCT) risk has focused on a possible perinatal etiology with a well-known hypothesis suggesting that hormonal involvement during fetal life is associated with risk. Second-to-fourth digit ratio (2D:4D) and left-hand dominance have been proposed as markers of prenatal hormone exposure. AIM: To evaluate associations between 2D:4D digit ratio, right minus left 2D:4D (DeltaR-L), and left-hand dominance and TGCT in the U.S. Servicemen’s Testicular Tumor Environmental and Endocrine Determinants Study. METHODS: A total of 246 TGCT cases and 236 non-testicular cancer controls participated in the current study, and completed a self-administered questionnaire. Associations between digit ratio, hand dominance and TGCT were estimated using unconditional logistic regression adjusting for identified covariates. RESULTS: Right 2D:4D was not associated with TGCT [odds ratio (OR) for a one-standard deviation (SD) increase in right-hand 2D:4D: 1.12, 95% confidence interval (CI): 0.93-1.34]. The results were consistent when evaluating the association based on the left hand. The difference between right and left-hand 2D:4D was also not associated with TGCT risk [OR for a one-SD increase in DeltaR-L: 1.03, 95% CI: 0.87-1.23]. Compared to men who reported right-hand dominance, ambidexterity [OR (95% CI)=0.65 (0.30-1.41)] and left-hand dominance [OR (95% CI)=0.79 (0.44-1.44)] were not associated with risk. CONCLUSIONS: These results do not support the hypothesis that prenatal hormonal imbalance is associated with TGCT risk. Given the limited sample
size, further evaluation of the relationship between TGCT and prenatal hormonal factors using digit ratio, DeltaR-L, or left-hand dominance and larger sample size are warranted.

[738]
**Título / Title:** Intra-abdominal mucinous adenocarcinoma of urachal origin: report of a case.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary


**Autores / Authors:** Hirashima K; Uchino R; Kume S; Iyama KI; Honda Y; Asato T; Baba H

**Institución / Institution:** Department of Surgery, Kumamoto City Ueki Hospital, 285-29 Iwano, Ueki-machi, Kita-ku, Kumamoto City, Kumamoto, 861-0136, Japan, gxrrm911@ybb.ne.jp.

**Resumen / Summary:** Intra-abdominal mucinous cystic tumors can be difficult to diagnose preoperatively. We report a case of histologically diagnosed primary urachal adenocarcinoma: a rare type of bladder tumor. This case report is interesting for clinicians. The patient was an 86-year-old man who presented with acute abdominal pain. Computed tomography (CT) showed a large cystic mass with calcification, near the apex of the urinary bladder. Laparotomy revealed a large intra-abdominal cystic mass adherent to the anterior abdominal wall and superior to the urinary bladder. We performed laparoscopic-assisted resection and partial cystectomy. The cystic mass measured approximately 15 x 14 x 11 cm and contained mucinous material. Histological examination revealed that it extended to the muscle of the bladder wall and that its epithelium was composed of atypical cells with increased papillary morphology. The mucinous material was glycoprotein with degenerative fatty tissue, and calcification was recognized partly in the specimen. Thus, we comprehensively diagnosed a mucinous cystic adenocarcinoma of urachal origin.

[739]
**Título / Title:** Effect of sarcosine on antioxidant parameters and metallothionein content in the PC-3 prostate cancer cell line.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary


**Enlace al texto completo (gratuito o de pago)** 3892/or.2013.2389
Sarcosine is currently one of the most discussed markers of prostate cancer. It is involved in amino acid metabolism and methylation processes that occur during the progression of prostate cancer. In this study, we monitored the effect of the addition of sarcosine (0; 10; 250; 500; 1,000 and 1,500 microM) in a time-dependent manner (0-72 h) on the PC-3 prostate cancer cell line. For the assessment of cell viability, the commonly used MTT test was employed. Furthermore, ion-exchange liquid chromatography was used for the determination of sarcosine content in the PC-3 cells. We also determined metallothionein (MT) levels by chip capillary electrophoresis and Brdicka reaction in the cells treated with sarcosine. Sarcosine levels in the cells increased in a concentration-dependent manner levels increased from only 270 nM with the lowest applied concentration of sarcosine (10 microM) to 106 microM with the highest applied concentration of sarcosine (1,500 microM). There was a marginal change observed in the MT concentration. Finally, the antioxidant activity of the PC-3 cells was determined using five different spectrophotometric methods [2,2-diphenyl-1-picrylhydrazyl (DPPH), ferric reducing ability of plasma (FRAP), free radicals, N,N-dimethyl-p-phenylenediamine (DMPD) and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid (ABTS)]. A significant negative correlation was observed between DPPH and FRAP (r=-0.68 at p<0.001) and between DMPD and ABST (r=-0.64 at p<0.001). Additionally, as regards the correlation between MT and DPPH, a significant positive trend (r=0.62 at p<0.001) was observed.
RESUMEN / SUMMARY: - INTRODUCTION: Radiolabeled Arg-Gly-Asp (RGD) and bombesin (BBN) heterodimers have been investigated for dual targeting of tumor integrin alphavbeta3 receptors and gastrin-releasing peptide receptors. The goal of this study was to evaluate the potential use of a Lu-labeled RGD-BBN heterodimer for targeted prostate cancer therapy. MATERIALS AND METHODS: A 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid-conjugated RGD-BBN peptide (DO3A-RGD-BBN) was radiolabeled with Lu and purified by high-performance liquid chromatography. The in-vivo biodistribution study of Lu-DO3A-RGD-BBN was carried out in mice bearing human prostate cancer PC3 xenografts. The receptor-targeting specificity of the radiolabeled peptide was assayed by injecting the tracer with the unlabeled RGD-BBN peptide. Radiation absorbed doses in adult male patients, based on biodistribution data from mice, were also calculated. RESULTS: DO3A-RGD-BBN peptides were successfully labeled with Lu, and high radiochemical purity (>95%) could be achieved after high-performance liquid chromatography purification. In human PC3 xenograft-bearing mice, the tumor accumulation of Lu-DO3A-RGD-BBN was 5.88+/−1.12, 2.77+/−0.30, 2.04+/−0.19, and 1.18+/−0.19%ID/g at 0.5, 2, 24, and 48 h, respectively. With rapid clearance from normal tissues, the radiolabeled probe displayed high tumor-to-blood and tumor-to-muscle ratios. On calculating the radiation absorbed doses for Lu-DO3A-RGD-BBN, we found that the prostate tumor and the pancreas were the organs receiving the highest radiation absorbed doses. CONCLUSION: Dual integrin alphavbeta3 and GPRP-targeted agent Lu-DO3A-RGD-BBN shows excellent prostate cancer-targeting ability, and it is worthy of further evaluation for prostate cancer-targeted therapy.

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TÍTULO / TITLE: - Severe retroperitoneal haemorrhage in the first trimester of a multiple pregnancy after spontaneous rupture of renal angiomyolipoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ferianec V; Gabor M; Cano M; Papcun P; Holoman K

INSTITUCIÓN / INSTITUTION: - 2nd Department of Obstetrics and Gynaecology, University Hospital Bratislava, Comenius University, Ruzinovska 6, Bratislava, Slovak Republic, ferianec@gmail.com.
TÍTULO / TITLE: Increasing Prostate-Specific Antigen Levels Differently Influence Prostate Cancer Detection Rates of Two Different 12-Core Prostate Biopsy Schemes.

RESUMEN / SUMMARY: Objective: To compare two 12-core transrectal ultrasound-guided prostate biopsy schemes in respect to cancer detection rates. Methods: Retrospective, single-center analysis of consecutive patients (n = 897) who underwent prostate biopsy (S1) with all 12 cores from far lateral areas (n = 269) or prostate biopsy (S2) with 6 cores from parasagittal and 6 from far lateral areas (n = 628). Results: Crude cancer detection rates with S1 and S2 were similar (39.0 and 38.9% for the first biopsy and 29.4 and 31.3% for repeated biopsies, respectively). Abnormal digital rectal exam, lower prostate volume and higher prostate-specific antigen (PSA) levels were independently associated with higher odds of cancer detection. Regarding first biopsies (n = 747), there was significant interaction between biopsy scheme and PSA (p < 0.001). Overall, the adjusted odds of cancer detection were higher with S1 (S1/S2 odds ratio = 2.54, 95% CI: 1.12-5.74), but the S1-S2 relationship was conditional on PSA: odds ratios progressively increased with increasing PSA from 0.64 (95% CI: 0.40-1.02) at PSA 5 ng/ml to 39.1 (95% CI: 2.71-566) at 75 ng/ml. Conclusion: Higher PSA levels increase the probability of cancer detection with 12-core prostate biopsies, but relative efficiency of different procedures appeared conditional on the PSA level. Data suggest that PSA levels should be considered in the choice of prostate biopsy sampling scheme.


NUEVA SECCIÓN: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Lodeta B; Benko G; Trkulja V

INSTITUCIÓN / INSTITUTION: - Department of Urology, General Hospital Varazdin, Varazdin, Croatia.

AUTORES / AUTHORS: - Li QQ; Wang G; Liang H; Li JM; Huang F; Agarwal PK; Zhong Y; Reed E

INSTITUCIÓN / INSTITUTION: - Beihai Institute of Endocrine and Metabolic Diseases, Beihai, Guangxi, PR China.
RESUMEN / SUMMARY: - Cisplatin-based combination treatment is the most effective systemic chemotherapy for bladder cancer; however, resistance to cisplatin remains a significant problem in the treatment of this disease. beta-Elemene is a new natural compound that blocks cell-cycle progression and has a broad spectrum of antitumor activity. This study was conducted to explore the potential of beta-elemene as a chemosensitizer for enhancing the therapeutic efficacy and potency of cisplatin in bladder cancer and other solid carcinomas. beta-Elemene not only markedly inhibited cell growth and proliferation but also substantially increased cisplatin cytotoxicity towards human bladder cancer 5637 and T-24 cells. Similarly, beta-elemene also enhanced cisplatin sensitivity and augmented cisplatin cytotoxicity in small-cell lung cancer and carcinomas of the brain, breast, cervix, ovary, and colorectal tract in vitro, with dose-modifying factors ranging from 5 to 124. beta-Elemene-enhanced cisplatin cytotoxicity was associated with increased apoptotic cell death, as determined by DNA fragmentation, and increased activities of caspase-3, -7, -8, -9, and -10 in bladder cancer cell lines. Collectively, these results suggest that beta-elemene augments the antitumor activity of cisplatin in human bladder cancer by enhancing the induction of cellular apoptosis via a caspase-dependent mechanism. Cisplatin combined with beta-elemene as a chemosensitizer warrants further pre-clinical therapeutic studies and may be useful for the treatment of cisplatin-resistant bladder cancer and other types of carcinomas.

[744]

TÍTULO / TITLE: - RADIATION EXPOSURE ASSOCIATED WITH DEDICATED RENAL MASS COMPUTER TOMOGRAPHY PROTOCOL: IMPACT OF PATIENT CHARACTERISTICS.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Tsivian M; Abern MR; Yoo J; Evans P; Qi P; Kim CY; Lipkin ME; Polascik TJ; Ferrandino MN

INSTITUCIÓN / INSTITUTION: - Duke University Medical Center, Division of Urology, Dept. of Surgery, DUMC Box 2804, Durham, North Carolina, United States, 27705 ; matvey.tsivian@duke.edu.

RESUMEN / SUMMARY: - Introduction: Renal mass protocol computed tomography (RMP-CT) using multiphase abdomen and pelvis CT imaging is the mainstay for diagnosis, characterization and follow-up for renal masses; however, it is associated with ionizing radiation to the patient. We sought to quantify the effective dose associated with RMP-CT and to determine how patient factors affect radiation exposure. Material and Methods: We retrospectively reviewed the records of 247 patients undergoing management of a small renal mass (cT1a) between 2005-2011 at our institution. BMI was
categorized as normal weight, overweight, obese and morbidly obese (\(<\!\!\!<25, 25.1-30, 30.1-35\) and \(>35\), respectively). Effective dose of RMP-CT was calculated through the dose-length-product multiplied by a factor coefficient (0.015). Effective doses in milliSieverts (mSv) were correlated to patient characteristics. Results: Patients’ median age was 61 years, median BMI 28.7 kg/m², 72% were Caucasian and 56% were male. Median effective dose was 26.1 mSv (IQR 20.6-35.3). When stratified by BMI, the median effective doses were 18.9, 25.2, 27.7 and 36.2 mSv for normal weight, overweight, obese and morbidly obese patients, respectively. On multivariable analyses, BMI and male gender were significantly associated with increased radiation dose. Conclusions: In this series the median effective dose for RMP-CT was 26.1 mSv. Obesity was independently associated with markedly increased radiation exposure, with morbidly obese patients being exposed to almost twice the amount of radiation compared to normal weight individuals. These findings should be considered when devising management strategies in patients with a renal mass and strategies should be developed to reduce medical ionizing radiation exposure.

[745]

**TÍTULO / TITLE:** - Quantification of candidate prostate cancer metabolite biomarkers in urine using dispersive derivatization liquid-liquid microextraction followed by gas and liquid chromatography-mass spectrometry.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Shamsipur M; Naseri MT; Babri M

**INSTITUCIÓN / INSTITUTION:** - Department of Chemistry, Razi University, Kermanshah, Iran. Electronic address: mshamsipur@yahoo.com

**RESUMEN / SUMMARY:** - A simple, rapid and sensitive method based on dispersive derivatization liquid-liquid microextraction (DDLLME) combined with gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS) was developed and validated for the determination of prostate cancer metabolite biomarkers, including sarcosine, alanine, leucine and proline, in human urine samples. Dispersive derivatization using isobutyl chloroformate has been successfully employed to identify the amino acids of interest in ng/mL(-1) concentrations. Under the optimum experimental conditions, the detection limits of the amino acids were in the range of 0.05-0.1 ng/mL(-1). The enrichment factor and relative recovery for the target amino acids were in the range of 140-155 and 93.8-106%, respectively. The proposed method showed good linearity (correlation coefficients >0.997), and good intra-day (below 7%) and inter-day precision (below 10%). This protocol provides a
rapid, simple, selective and sensitive tool to quantify sarcosine and endogenous urinary metabolite for prostate cancer diagnosis and for a screening test.

[746]
TITULO / TITLE: MicroRNA-21 is overexpressed in renal cell carcinoma.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Lv L; Huang F; Mao H; Li M; Li X; Yang M; Yu X
INSTITUCIÓN / INSTITUTION: Department of Nephrology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou - China.
RESUMEN / SUMMARY: Objective: To identify microRNAs (miRNAs) that are overexpressed in renal cell carcinoma (RCC) and characterize the functional role of miR-21.

Materials and methods: The miRNA expression profiles between RCC tissue and adjacent normal tissue were compared using microarray analysis. The differential expression of miR-21 was validated by real-time polymerase chain reaction (RT-PCR). 786-O RCC cells were transfected with miR-21 mimic, miR-21 inhibitor, or negative controls and cell proliferation, apoptosis and cell cycle were examined by MTT assay and flow cytometry. The expression of programmed cell death 4 (PDCD4) and tropomyosin 1 (TPM1) was detected by RT-PCR and Western blot analysis.

Results: Compared to adjacent normal tissue, 10 human miRNAs were significantly upregulated and 7 were downregulated in RCC tissue. RT-PCR confirmed that miR-21 was significantly overexpressed in RCC tissue. In vitro expression of miR-21 mimic promoted the growth of 786-O cells, whereas miR-21 inhibitor inhibited cell growth by inducing apoptosis and cell cycle arrest at S phase. Furthermore, miR-21 mimic or inhibitor significantly reduced or increased the expression of PDCD4 and TPM1.

Conclusions: MiR-21 is overexpressed in RCC tissue and modulates the growth, apoptosis and cell cycle progression of RCC cells and regulates the expression of PDCD4 and TPM1.

[747]
TITULO / TITLE: miR-708 promotes the development of bladder carcinoma via direct repression of Caspase-2.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Song T; Zhang X; Zhang L; Dong J; Cai W; Gao J; Hong B
RESUMEN / SUMMARY: - PURPOSE: Bladder cancer is one of the world’s top ten malignant tumors. The crucial role of microRNA in carcinogenesis has been well emphasized. Considering miRNA expression was tumor stage-, tissue-, or even development-specific, more experimental evidences about the functions of miRNAs in bladder cancer should be discovered to advance applying of miRNA in the diagnosis or therapy of cancer. METHODS: MiR-708 level in bladder carcinoma and adjacent noncancerous tissues was tested by real-time qPCR. Cell apoptosis was analyzed by using flow cytometry. The tumorigenicity of bladder carcinoma cells was evaluated in nude mice model. Luciferase reporter gene assays were performed to identify the interaction between miR-708 and 3’UTR of Caspase-2 mRNA. The protein level of Caspase-2 was determined by western blotting. RESULTS: In this study, we reported that miR-708 was frequently dysregulated in human bladder carcinoma tissues compared to normal tissues. In addition, we found that silencing of miR-708 could promote the T24 and 5637 cells to apoptosis and inhibit the bladder tumor growth in vivo. Also, Caspase-2 was proved to be one of direct targets of miR-708 in T24 and 5637 cells. Further results showed that Caspase-2 was involved in the miR-708 regulated cell apoptosis. CONCLUSIONS: All together, these results suggest miR-708 may act as an oncogene and induce the carcinogenicity of bladder cancer by down-regulating Caspase-2 level.
2 weeks for 6 doses. Group 1 received a peptide presented by an HLA class I haplotype (HLA-A2), Group 2 with a peptide presented by HLA class II haplotype (DR4, DP4), and Group 3 with peptides presented by both Class I and II haplotypes. Androgen-deprivation was continued. Owing to a myocardial infarction, the protocol was amended to omit the use of GM-CSF. Results Fourteen patients were evaluable for toxicities and 9 received all 6 doses and were evaluable for efficacy. One death from myocardial infarction following GM-CSF occurred in a patient with generalized myalgias. After omitting GM-CSF, no grade >2 toxicities were observed. Among 9 patients evaluable for efficacy, the median PSA doubling time pre-therapy and during therapy were 3.1 and 4.92 months, respectively. NY-ESO-1 specific T-cell response observed by ELISPOT appeared more frequent in docetaxel-naive patients (4 of 4) than docetaxel-pretreated patients (2 of 5). Conclusion In men with mCRPC, individualized HLA class-I and/or class-II restricted NY-ESO-1 peptides were tolerable, appeared to slow PSA doubling time and yielded antigen-specific T-cell responses more often in chemonaive patients.

[749]

TÍTULO / TITLE: - Leydig cell tumor in an anabolic steroid abuser.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Belli S; Guidi A; Simoni M; Carani C; Granata AR
INSTITUCIÓN / INSTITUTION: - Division of Endocrinology, Department of Medicine, Endocrinology & Metabolism, Geriatrics, University of Modena & Reggio Emilia, Italy.

[750]

TÍTULO / TITLE: - Bladder carcinoma in situ (CIS) in Australia: a rising incidence for an under-reported malignancy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ranasinghe WK; Attia J; Oldmeadow C; Lawrentschuk N; Robertson J; Ranasinghe T; Bolton D; Persad R
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Urology Unit, Austin Hospital, Heidelberg, Victoria.
RESUMEN / SUMMARY: - OBJECTIVES: To investigate the incidence of carcinoma in situ (CIS) in Australia and examine implications for its diagnosis and management, as CIS of the urinary bladder is a non-reportable disease in Australia. METHODS: Analysis of annual hospitalisation data using Australian
Institute of Health and Welfare (AIHW) datasets showed an increase in CIS from 2001 onwards. To determine whether the increase seen with AIHW data represented a true increase in the rates of CIS, patient level data was examined using the Centre for Health record linkage (CHeReL) datasets. RESULTS: CHeReL linked data of 13,790 males and 5,902 females, calculated the average incidence of CIS to be 20.9 per 100,000 and 6.5 per 100,000 respectively in those aged > 50 years, showing a rapid increase in the rates of CIS from 2001. There was an 11% (P = 0.04) and 14% (P = 0.02) annual increase in incidence of CIS in men and women and these rates increased with age. CONCLUSIONS: National data (AIHW) substantially underestimate the incidence of CIS in the Australian population. Patient level data suggest CIS rates are rapidly increasing in Australia despite high treatment rates. Closer surveillance and awareness of these high rates warrants further study and we recommend that CIS be considered a reportable disease.

[751]

**TÍTULO / TITLE:** - Pathology of renal cell carcinoma: an update.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Lopez-Beltran A; Cheng L; Vidal A; Scarpelli M; Kirkali Z; Blanca A; Montironi R

**INSTITUCIÓN / INSTITUTION:** - Anatomical Pathology Unit, Department of Surgery, Faculty of Medicine, University of Cordoba, Cordoba, España. em1lobea@uco.es

**RESUMEN / SUMMARY:** - The use of classic and newer methodologies, including histopathology, electron microscopy, immunohistochemistry, cytogenetics, and molecular diagnostic techniques, has greatly influenced distinctions between various types of renal carcinoma. The most recent World Health Organization classification of renal neoplasms encompassed nearly 50 distinctive renal neoplasms. These categories have been expanded during recent years, incorporating newer histotypes, thus suggesting that the next revision of this classification will incorporate some of the recently recognized entities. In this review we examine the clinicopathologic and genetic features of renal carcinomas most often seen in clinical practice. Emphasis is placed on defining risk categories by incorporating pathologic predictive paradigms and tumor histotypes. Since pathology of renal cell cancer is a rapidly evolving field, we also include brief comments on newer tumor variants for which there currently is not enough clinicopathologic information to permit classification as distinctive tumor histotypes.

[752]
**TITULO / TITLE:** - Downregulation of microRNA-29c is associated with renal failure in multiple myeloma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Leuk Lymphoma. 2013 May 9.
- Enlace al texto completo (gratuito o de pago) 3109/10428194.2013.800199

**AUTORES / AUTHORS:** - Zhang S; Wu S; Qu X; Zhao M; Xu J; Jianyong L; Lijuan C

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**TITULO / TITLE:** - Liposarcoma of the spermatic cord: an unexpected finding of inguinal hernia repair.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Bhullar JS; Mohey L; Chaudhary S; Herschman B; Ferguson L

**INSTITUCION / INSTITUTION:** - Department of Surgery, Providence Hospital and Medical Centers, Southfield, Michigan, USA.

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**TITULO / TITLE:** - Intratumoral inflammation is associated with more aggressive prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - World J Urol. 2013 Apr 2.
- Enlace al texto completo (gratuito o de pago) 1007/s00345-013-1065-8

**AUTORES / AUTHORS:** - Klink JC; Banez LL; Gerber L; Lark A; Vollmer RT; Freedland SJ

**INSTITUCION / INSTITUTION:** - Urology Section, Department of Surgery, Veterans Affairs Medical Center, Durham, NC, USA, klinkj@ccf.org.

**RESUMEN / SUMMARY:** - PURPOSE: Inflammation may play a role in the development and progression of many cancers, including prostate cancer. We sought to test whether histological inflammation within prostate cancer was associated with more aggressive disease. METHODS: The slides of prostatectomy specimens were reviewed by a board-certified pathologist on 287 men from a Veterans Affairs Medical Center treated with radical prostatectomy from 1992 to 2004. The area with the greatest tumor burden was scored in a blinded manner for the degree of inflammation: absent, mild, or marked. We used logistic and Cox proportional hazards regression analysis to examine whether categorically coded inflammation score was associated with adverse pathology and biochemical progression, respectively. RESULTS: No
inflammation was found in 49 men (17%), while 153 (53%) and 85 (30%) had mild and marked inflammation. During a median follow-up of 77 months, biochemical recurrence occurred among 126 (44%) men. On multivariate analysis, more inflammation was associated with greater risk of positive margins, capsular penetration, and seminal vesicle invasion (all p < 0.05). Marked inflammation was associated with increased PSA recurrence risk when adjusting for preoperative features only (HR 2.08, 95% CI 1.02-4.24), but not after adjusting for pathologic features. CONCLUSIONS: Inflammation within prostate cancer was associated with more advanced disease, although it is unclear whether aggressive disease caused increased inflammation or inflammation caused aggressive disease.

[755]

TÍTULO / TITLE: - PET Imaging in Prostate Cancer: Focus on Prostate-Specific Membrane Antigen.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Mease RC; Foss CA; Pomper MG
INSTITUCIÓN / INSTITUTION: - Russell H. Morgan Department of Radiology and Radiological Science, CRBII, 1550 Orleans Street, Baltimore, MD 21231, USA. mpomper@jhmi.edu.
RESUMEN / SUMMARY: - Prostate cancer (PCa) is the second leading cause of cancer-related death in American men. Positron emission tomography/computed tomography (PET/CT) with emerging radiopharmaceuticals promises accurate staging of primary disease, restaging of recurrent disease, detection of metastatic lesions and, ultimately, for predicting the aggressiveness of disease. Prostate-specific membrane antigen (PSMA) is a well-characterized imaging biomarker of PCa. Because PSMA levels are directly related to androgen independence, metastasis and progression, PSMA could prove an important target for the development of new radiopharmaceuticals for PET. Preclinical data for new PSMA-based radiotracers are discussed and include new (89)Zr- and (64)Cu-labeled anti-PSMA antibodies and antibody fragments, (64)Cu-labeled aptamers, and (11)C-, (18)F-, (68)Ga-, (64)Cu-, and (86)Y-labeled low molecular weight inhibitors of PSMA. Several of these agents, namely (68)Ga- HBED-CC conjugate 15, (18)F-DCFBC 8, and BAY1075553 are particularly promising, each having detected sites of PCa in initial clinical studies. These early clinical results suggest that PET/CT using PSMA-targeted agents, especially with compounds of low molecular weight, will make valuable contributions to the management of PCa.
[756] **TÍTULO / TITLE:** Trends in the surgical management of localized renal masses.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
★•Enlace al texto completo (gratuito o de pago) 1111/j.1464
410X.2012.11509.x
**AUTORES / AUTHORS:** Bolton DM
**INSTITUCIÓN / INSTITUTION:** University of Melbourne, Austin Hospital, Melbourne, Australia. damienmb@unimelb.edu.au.

[757] **TÍTULO / TITLE:** Critical role of TRPC6 channels in the development of human renal cell carcinoma.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
★•Enlace al texto completo (gratuito o de pago) 1007/s11033-013-2613-4
**AUTORES / AUTHORS:** Song J; Wang Y; Li X; Shen Y; Yin M; Guo Y; Diao L; Liu Y; Yue D
**INSTITUCIÓN / INSTITUTION:** School of Laboratory Medicine, Tianjin Medical University, Tianjin, 300203, China.
**RESUMEN / SUMMARY:** Renal cell carcinoma (RCC) is the most common tumor arising from the cells in the lining of tubules in the kidney. Some members of the Ca2+-permeable transient receptor potential canonical (TRPC) family of channel proteins have demonstrated a role in the proliferation of some types of cancer cells. In this study, we investigated the role of TRPC6 in the development of human RCC. RT-PCR and Western blotting were used to investigate TRPC6 expression in 1932 and ACHN cells. Immunohistochemical techniques were applied to study TRPC6 expression in 60 cases of RCC primary tissue samples and 10 cases of corresponding normal renal tissues. To inhibit TRPC6 activity or expression, RNA interference was used. The effects of TRPC6 channels on RCC cell viability and cell cycle progression were investigated by MTT and flow cytometry. TRPC6 was expressed in 1932 and ACHN cells. TRPC6 protein was detected in 73.3 % of RCC samples, and there was a significant difference compared with the normal renal samples (30 %) (p < 0.05). Moreover the level of TRPC6 expression was associated with RCC Fuhrman grade (p < 0.01). Blockade of TRPC6 channels in ACHN cells suppressed basal cell proliferation and partially inhibited HGF-induced cell proliferation. Furthermore, inhibition of TRPC6 channels expression prolonged the transition through G2/M phase in ACHN cells. In summary, expression of
TRPC6 is markedly increased in RCC specimens and associated with RCC histological grade. TRPC6 plays an important role in ACHN cells proliferation.

[758]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago)
1097/COC.0b013e318294101b
AUTORES / AUTHORS: - Collins SP; Suy S; Chen LN; Collins BT; Dritschilo A
INSTITUCIÓN / INSTITUTION: - Department of Radiation Medicine Georgetown University Hospital Washington, DC.

[759]
TÍTULO / TITLE: - Infantile neuroblastoma of the urinary bladder detected by hematuria.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1007/s00383-013-3305-9
AUTORES / AUTHORS: - Kojima SI; Yagi M; Asagiri K; Fukahori S; Tanaka Y; Ishii S; Saikusa N; Koga Y; Yoshida M; Masui D; Komatsuzaki N; Nakagawa SI; Ozono S; Tanikawa K
INSTITUCIÓN / INSTITUTION: - Department of Pediatric Surgery, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka, 830-0011, Japan, kojima_shinichirou@med.kurume-u.ac.jp.
RESUMEN / SUMMARY: - Malignant tumors of the urinary bladder in infants are extremely rare. Rhabdomyosarcoma is the most likely tumor in this site, whereas neuroblastoma of the urinary bladder is exceedingly uncommon and is not listed as a differential diagnosis for tumors of this site. We present a case of neuroblastoma arising from the dome of the bladder wall, detected by hematuria. Only six cases of neuroblastoma originating from the bladder, including the present case have been reported. Of the cases, five arose from the dome of the bladder wall. In this report, the differential diagnosis of bladder tumors in children is discussed. A diagnosis of neuroblastoma should be taken into consideration, especially in the case of tumors arising from the dome of the bladder wall despite an uncommon location.

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RELACIÓN ENTRE NIVELES DE ANTÍGENO ESPECÍFICO DE PROSTATA Y TEMPERATURA AMBIENTAL.

RESUMEN / SUMMARY:

Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL:


●●Enlace al texto completo (gratuito o de pago) 1007/s00484-013-0644-0

AUTORES / AUTHORS:

Ohwaki K; Endo F; Hattori K; Muraishi O

INSTITUCIÓN / INSTITUTION:

Department of Hygiene and Public Health, Teikyo University School of Medicine, 2-11-1 Kaga, Itabashi-ku, Tokyo, 173-8605, Japan, ns-waki@med.teikyo-u.ac.jp.

RESUMEN / SUMMARY:

We examined the association between prostate-specific antigen (PSA) and daily mean ambient temperature on the day of the test in healthy men who had three annual checkups. We investigated 9,694 men who visited a hospital for routine health checkups in 2007, 2008, and 2009. Although the means and medians of ambient temperature for the three years were similar, the mode in 2008 (15.8 degrees C) was very different from those in 2007 and 2009 (22.4 degrees C and 23.2 degrees C). After controlling for age, body mass index, and hematocrit, a multiple regression analysis revealed a U-shaped relationship between ambient temperature and PSA in 2007 and 2009 (P < 0.001 and P = 0.004, respectively), but not in 2008 (P = 0.779). In 2007, PSA was 13.5 % higher at 5 degrees C and 10.0 % higher at 30 degrees C than that at 18.4 degrees C (nadir). In 2009, PSA was 7.3 % higher at 5 degrees C and 6.8 % at 30 degrees C compared with the level at 17.7 degrees C (nadir). In logistic regression analysis, a U-shaped relationship was found for the prevalence of a higher PSA (> 2.5 ng/mL) by ambient temperature, with the lowest likelihood of having a high PSA at 17.8 degrees C in 2007 (P = 0.038) and 15.5 degrees C in 2009 (P = 0.033). When tested at 30 degrees C, there was a 57 % excess risk of having a high PSA in 2007 and a 61 % higher risk in 2009 compared with those at each nadir temperature. We found a U-shaped relationship between PSA and ambient temperature with the lowest level of PSA at 15-20 degrees C.

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EL Rol DE LA INFLAMACIÓN CRÓNICA DE LA PROSTATA EN LA PATHOGNÉSIS Y PROGRESIÓN DE LA HIPERPLASIA BENIGNA DE LA PROSTATA (BPH).

RESUMEN / SUMMARY:

Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL:


●●Enlace al texto completo (gratuito o de pago) 1111/bju.12118

AUTORES / AUTHORS:

Gandaglia G; Briganti A; Gontero P; Mondaini N; Novara G; Salonia A; Sciarra A; Montorsi F
INSTITUCIÓN / INSTITUTION: - Department of Urology, Urological Research Institute, University Vita-Salute San Raffaele, San Raffaele Scientific Institute, Milan.

RESUMEN / SUMMARY: - Several different stimuli may induce chronic prostatic inflammation, which in turn would lead to tissue damage and continuous wound healing, thus contributing to prostatic enlargement. Patients with chronic inflammation and benign prostatic hyperplasia (BPH) have been shown to have larger prostate volumes, more severe lower urinary tract symptoms (LUTS) and a higher probability of acute urinary retention than their counterparts without inflammation. Chronic inflammation could be a predictor of poor response to BPH medical treatment. Thus, the ability to identify patients with chronic inflammation would be crucial to prevent BPH progression and develop target therapies. Although the histological examination of prostatic tissue remains the only available method to diagnose chronic inflammation, different parameters, such as prostatic calcifications, prostate volume, LUTS severity, storage and prostatitis-like symptoms, poor response to medical therapies and urinary biomarkers, have been shown to be correlated with chronic inflammation. The identification of patients with BPH and chronic inflammation might be crucial in order to develop target therapies to prevent BPH progression. In this context, clinical, imaging and laboratory parameters might be used alone or in combination to identify patients that harbour chronic prostatic inflammation.

[762]
TÍTULO / TITLE: - A novel oncocytoid papillary renal cell carcinoma, type 2, with aberrant cytogenetic abnormalities: oncocytic papillary renal cell carcinoma?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Hes O; Brunelli M; Hora M; Michal M
INSTITUCIÓN / INSTITUTION: - *Departments of Pathology daggerUrology, Charles University, Medical Faculty and Charles University Hospital Plzen, Czech Republic double daggerDepartment of Pathology, University Hospital Verona, Verona, Italy.

[763]
TÍTULO / TITLE: - Development, characterization and application of a new fibroblastic-like cell line from kidney of a freshwater air breathing fish Channa striatus (Bloch, 1793).
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

565
RESUMEN / SUMMARY: - A new cell line, Channa striatus kidney (CSK), derived from the kidney tissue of murrel, was established and characterized. The CSK cell line was maintained in Leibovitz’s L-15 supplemented with 10% fetal bovine serum and has been subcultured more than 140 times. This cell line was able to grow in a range of temperatures from 22 to 32 degrees C with optimal growth at 28 degrees C. The plating efficiency was very high (67.54%) and doubling time was approximately 29h. The kidney cell line was cryopreserved at different passage levels and revived successfully with 90-92% survival. Polymerase chain reaction amplification of mitochondrial 16S rRNA using primer specific to C. striatus confirmed the origin of this cell line from murrel. The cell line was further characterized by chromosome number, transfection and mycoplasma detection. A marine fish nodavirus was tested to determine the susceptibility of this new cell line. The CSK cell line was found to be susceptible to nodavirus and the infection was confirmed by cytopathic effect (CPE), reverse transcriptase-polymerase chain reaction (RT-PCR), immunodot blot, enzyme linked immunosorbent assay (ELISA), virus replication efficiency and real time RT-PCR. The present study highlights the development and characterization of a new kidney cell line from an air breathing fish that could be used as an in vitro tools for propagation of fish viruses and gene expression studies.
rodent testis, however, its presence in the human testis and in testicular germ cell tumors is not known. We used RT-PCR and immunohistological observations to investigate whether human testicular tissue and testicular germ cell tumors contain PACAP. The mRNAs for PACAP and its receptors were detected in total RNA extracted from human testes. PACAP immunoreactivity was observed in spermatogonia and spermatids from normal testes. In contrast, diffuse PACAP immunopositivity was observed in seminoma tumor cells, while only faint immunoreactivity was observed in embryonal carcinoma cells. Our data suggest that PACAP may play a role in human spermatogenesis and in testicular germ cell tumor development.

[765]

TÍTULO / TITLE: - Why prostate tumour delineation based on apparent diffusion coefficient is challenging: An exploration of the tissue microanatomy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Borren A; Moman MR; Groenendaal G; Boeken Kruger AE; van Diest PJ; van der Groep P; van der Heide UA; van Vulpen M; Philippens ME

INSTITUCIÓN / INSTITUTION: - Department of Radiotherapy, University Medical Center Utrecht, Utrecht, The Netherlands.

RESUMEN / SUMMARY: - Background. Focal boosting of prostate tumours to improve outcome, requires accurate tumour delineation. For this, the apparent diffusion coefficient (ADC) derived from diffusion-weighted MR imaging (DWI) seems a useful tool. On voxel level, the relationship between ADC and histological presence of tumour is, however, ambiguous. Therefore, in this study the relationship between ADC and histological variables was investigated on voxel level to understand the strengths and limitations of DWI for prostate tumour delineation. Material and methods. Twelve radical prostatectomy patients underwent a pre-operative 3.0T DWI exam and the ADC was calculated. From whole-mount histological sections cell density and glandular area were retrieved for every voxel. The distribution of all variables was described for tumour, peripheral zone (PZ) and central gland (CG) on regional and voxel level. Correlations between variables and differences between regions were calculated. Results. Large heterogeneity of ADC on voxel level was observed within tumours, between tumours and between patients. This heterogeneity was reflected by the distribution of cell density and glandular area. On regional level, tumour was different from PZ having higher cell density (p = 0.007), less glandular area (p = 0.017) and lower ADCs (p = 0.017). ADC was correlated with glandular area (r = 0.402) and tumour volume (r = -0.608),
but not with Gleason score. ADC tended to decrease with increasing cell density ($r = -0.327, p = 0.073$). On voxel level, correlations between ADC and histological variables varied among patients, for cell density ranging from $r = -0.439$ to $r = 0.261$ and for glandular area from $r = 0.593$ to $r = 0.207$.

Conclusions. The variation in ADC can to a certain extent be explained by the variation in cell density and glandular area. The ADC is highly heterogeneous, which reflects the heterogeneity of malignant and benign prostate tissue. This heterogeneity might however obscure small tumours or parts of tumours. Therefore, DWI has to be used in the context of multiparametric MRI.
radiotherapy. Here we provide a review of the main important immune treatments in CRPC.

[767]

**TITULO / TITLE:** - Impact of tumour morphology on renal function decline after partial nephrectomy.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#).


**AUTORES / AUTHORS:** - Mehrazin R; Palazzi KL; Kopp RP; Colangelo CJ; Stroup SP; Masterson JH; Liss MA; Cohen SA; Jabaji R; Park SK; Patterson AL; L'esperance JO; Derweesh IH

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, University of Tennessee Health Science Center, Memphis, TN, USA.

**RESUMEN / SUMMARY:** - OBJECTIVE: To examine the association of renal morphology with renal function after partial nephrectomy (PN). PATIENTS AND METHODS: We conducted a multi-institutional retrospective analysis of 322 PNs performed between 2003 and 2011. The RENAL nephrometry score for each lesion was determined and the estimated glomerular filtration rate (eGFR) was calculated preoperatively and at last follow-up. We divided patients into two RENAL nephrometry score groups, low (<8) and high (≥8), and analysed and compared the outcomes of each group. The primary outcome was median change in eGFR between preoperative and last follow-up (DeltaeGFR). The secondary outcome was eGFR <60 mL/min/1.73 m² at last follow-up. Multivariable analysis was conducted to evaluate the risk factors for eGFR <60 mL/min/1.73 m² at last follow-up. RESULTS: The median (interquartile range) follow-up was 25.2 (13.5-39.3) months. Low (n = 165) and high (n = 157) RENAL score groups were well-matched for baseline eGFR. The median tumour size (4.2 vs 2.4 cm, P < 0.001) was greater for the high group. In all, 64% of the low and 88.2% of the high RENAL score group (P < 0.001) had decreased eGFR at last follow-up. Median eGFR was -7 for the low vs -13.8 mL/min/1.73 m² for the high group (P = 0.001); eGFR <60 mL/min/1.73 m² at last follow-up was 27.3% for the low vs 37.6% for the high group (P = 0.057). Linear regression analysis showed that for each 1-point increase in RENAL score, there was 2.5% decrease in eGFR (P = 0.002); for each 1-cm increase in tumour size, there was 1.8% decrease in eGFR (P = 0.013). Area under curve analyses showed no significant difference between RENAL score and tumour size for prediction of de novo eGFR <60 mL/min/1.73 m² (P = 0.920) and DeltaeGFR ≥50% (P = 0.85). Multivariable analysis showed that increasing RENAL score (odds ratio [OR] 1.24, P = 0.046) and decreasing preoperative eGFR (OR 1.10, P < 0.001) were risk factors for eGFR <60 mL/min/1.73 m² at
last follow-up. CONCLUSIONS: Increasing RENAL nephrometry score is an independent risk factor for eGFR <60 mL/min/1.73 m(2) after PN. RENAL nephrometry score may serve as an additional measure for risk stratification before PN, but further investigation is required.

[768]
TÍTULO / TITLE: - Genotoxic effects induced by zearalenone in a human embryonic kidney cell line.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Gao F; Jiang LP; Chen M; Geng CY; Yang G; Ji F; Zhong LF; Liu XF
INSTITUCIÓN / INSTITUTION: - Department of Nutrition and Food Safety, Dalian Medical University, No. 9, West Segment of South Lvshun Road, Dalian 116044, Liaoning, PR China.
RESUMEN / SUMMARY: - Mycotoxins are considered to be significant contaminants of food and animal feed. Zearalenone (ZEA) is a hepatotoxic mycotoxin with estrogenic and anabolic activity found in cereal grains worldwide. ZEA affects hematological and immunological parameters in humans and rodents. The compound can induce cell death, cause lipid peroxidation, inhibit protein and DNA synthesis, and exert genotoxic effects. ZEA may cause increased phagolysosomal fragility in the kidney. Our research showed that exposure of human embryonic kidney (HEK293) cells to ZEA (10 or 20μM) resulted in a concentration-dependent increase in DNA strand breaks measured with the comet assay. Damage was reduced in cells pretreated with NH4Cl, pepstatin A, or desipramine for 1h. Production of reactive oxygen species (ROS) was increased in cells exposed to ZEA, but DNA strand break induction could not be inhibited by the antioxidant hydroxytyrosol (HT). These results suggest that oxidative stress does not play a key role in DNA strand breaks induced by ZEA, that lysosomal injury precedes DNA strand breaks, and that the lysosome may be a primary target for ZEA in HEK293 cells.

[769]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Novel imaging techniques reshape the landscape in high-risk prostate cancers.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Lecouvet FE; Lhommel R; Pasoglou V; Larbi A; Jamar F; Tombal B
PURPOSE OF REVIEW: High-risk prostate cancers (PCa), that is, those with prostate-specific antigen greater than 20 ng/dl, Gleason Score of at least 8, or extraprostatic spread, are nowadays commonly treated by surgery and radiotherapy combined with a fixed period of systemic treatment. Implementing these strategies requires an exhaustive assessment of metastatic spread. This review addresses the latest development in integrated imaging techniques.

RECENT FINDINGS: In contrast to the progress that has been made in PCa treatment, diagnostic strategies have not much evolved. Most guidelines still recognize Tc bone scintigraphy and computed tomography (CT) as cornerstone modalities to assess metastatic spread in bones and lymph nodes. Therefore, modern imaging techniques should primarily focus on these two targets. PET with various tracers, including C or F-choline and F-sodium fluoride, and MRI with or without diffusion-weighted imaging are competing to supplant bone scan and CT scan as reference imaging techniques. This review focuses on the latest development of these techniques and analyses their potential impact in everyday urology practice.

SUMMARY: Although certain hurdles remain, PET and whole-body MRI have the ability to supplant Tc bone scan and CT as upfront test to assess metastatic spread in high-risk PCa.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Welk B; McIntyre A; Teasell R; Potter P; Loh E
RESUMEN / SUMMARY: Study design: Prospective scoping review. Objectives: To conduct a scoping review of all the literature related to bladder cancer in individuals with spinal cord injuries (SCI). Methods: Literature search of the databases Pubmed, CINAHL, ProQuest, PsychINFO and Scopus up to and including August 2012. Articles related to bladder cancer among SCI patients were identified, and data pertaining to epidemiology, risk factors, screening, prevention and management was reviewed and summarized. Results: An association between bladder cancer and SCI was first reported in the 1960s, with some case reports suggesting an alarmingly high rate among SCI patients. More recent epidemiological studies have reported this risk to be substantially
lower. However, bladder cancer in SCI patients tends to present at an earlier age and at a more advanced pathological stage than bladder cancer in the general population. Presenting symptoms may be atypical, and early recognition is important to improve prognosis with surgical resection. Several risk factors have been identified, including indwelling catheters, urinary tract infections and bladder calculi. Screening of SCI patients for bladder cancer is routinely recommended in many SCI management guidelines and by expert consensus; however, evidence for screening tools and protocols is lacking. Conclusion: Bladder cancer is a rare, and potentially lethal occurrence in SCI patients. Physicians need to have a high index of suspicion for bladder cancer, particularly among SCI patients managed with long-term indwelling catheters. Spinal Cord advance online publication, 23 April 2013; doi:10.1038/sc.2013.33.

[772] TÍTULO / TITLE: - Effect of belly board with bladder compression device on small bowel displacement from the radiotherapy field for rectal cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Chung Y; Yoon HI; Keum KC; Kim JH; Choi WH; Nam KC; Koom WS
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Yonsei University College of Medicine, Seoul, South Korea.
RESUMEN / SUMMARY: - Background: The aim of this study was to investigate the effect of a belly board (BB) with the addition of a bladder compression device (BCD) for small bowel (SB) displacement from the radiotherapy field for rectal cancer. Patients and Methods: Computed tomography (CT) scans of 38 rectal cancer patients positioned on a BB were analyzed and compared with CT scans from the same patients after the addition of a BCD. The BCD moves the inferior border of the BB from the pubic symphysis to the lumbosacral junction. The treated and irradiated volumes of the SB and bladder were compared. The irradiated volume ratio of SB to abdominopelvic cavity (APC) and that of bladder to APC were analyzed. Results: With the BCD, the treated and irradiated volumes of SB decreased significantly (49.1 +/- 48.0 vs. 60.9 +/- 50.9 cc, p = 0.006 and 207.5 +/- 140.8 vs. 482.8 +/- 214.2 cc, p < 0.001, respectively). The irradiated volume ratio of bladder to APC with the BCD increased considerably compared to that without the BCD (25.2 +/- 11.5 vs. 18.7 +/- 10.5%, p < 0.001), and the ratio of irradiated volume of SB to APC decreased significantly with the BCD (18.8 +/- 12.4 vs. 31.8 +/- 12.1%, p < 0.001). Conclusion: This study
showed that the addition of a BCD to the BB could effectively provide further displacement of SB from the rectal cancer radiotherapy field.

[773]
**TÍTULO / TITLE:** - Apocynin, an NADPH oxidase inhibitor, suppresses progression of prostate cancer via Rac1 dephosphorylation.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Suzuki S; Pitchakarn P; Sato S; Shirai T; Takahashi S

**INSTITUCIÓN / INSTITUTION:** - Department of Experimental Pathology and Tumor Biology, Graduate School of Medicine, Nagoya City University, Nagoya, Japan; Pathology Division, Nagoya City East Medical Center, Nagoya, Japan. Electronic address: shugo@med.nagoya-cu.ac.jp.

**RESUMEN / SUMMARY:** - Recently, considerable evidence has been generated that oxidative stress contributes to the etiology and pathogenesis of prostate cancer. The present study focused on the effects of apocynin, an inhibitor of the NADPH oxidase which generates intracellular superoxide, on a rat androgen-independent prostate cancer cell line (PLS10) in vitro and in vivo. Apocynin significantly inhibited cell proliferation of PLS10 cells via G1 arrest of the cell cycle in vitro. Surprisingly, it did not affect reactive oxygen species (ROS) but inhibited phosphorylation of Rac1, one component of the NADPH oxidase complex. A Rac1 inhibitor, NSC23766, also inhibited cell proliferation, and both apocynin and NSC23766 reduced phosphorylation of Rac1 and NF-kappaB, as well as cyclin D1. Furthermore, in a xenograft model of prostate cancer with PLS10, apocynin suppressed tumor growth and metastasis in a dose dependent manner in vivo, with reduction of cell proliferation and vessel number in the tumors. Expression and secretion of vascular endothelial growth factor (VEGF) were reduced by apocynin treatment in vivo and in vitro, respectively. In conclusion, despite no apparent direct relationship with oxidative stress, apocynin inhibited growth of androgen-independent prostate cancer in vitro and in vivo. Apocynin thus warrants further attention as a potential anti-tumor drug.

[774]
**TÍTULO / TITLE:** - Inhibition of ADAM-17 more effectively down-regulates the Notch pathway than that of gamma-secretase in renal carcinoma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 1186/1756-9966-32-26
AUTORES / AUTHORS: - Guo Z; Jin X; Jia H

INSTITUCIÓN / INSTITUTION: - Minimally Invasive Urology Center, Provincial Hospital Affiliated to Shandong University, No, 324 Jingwu Road, Jinan 250001, China. 944172919@qq.com.

RESUMEN / SUMMARY: - BACKGROUND: Our study is to research the effect of inhibited ADAM-17 expression through the Notch pathway in renal carcinoma.

METHODS: Immunohistochemistry and western blot were used to examine the expression of ADAM-17 protein in renal cancer tissues. Proliferation and cell invasion of 786-o cells, as well as OS-RC-2 cells, after treatment with two different inhibitors of the Notch pathway, were examined by CCK-8 assay and Transwell assay, respectively. 786-o cell apoptosis was measured using the FCM test.

RESULTS: ADAM-17 was highly expressed in RCC tissues. Compared with blocking gamma-secretase, a known mechanism of impairing Notch, blockade of ADAM-17 more effectively down-regulated the expressions of Notch1 and HES-1 proteins. Similarly, we found that the ADAM-17 inhibitor, Marimastat, could more efficiently reduce renal cell proliferation and invasive capacity in comparison with the gamma-secretase inhibitor DAPT when used at the same dose. Similar results were obtained when apoptosis of 786-o was measured.

CONCLUSION: Compared with gamma-secretase, inhibition of ADAM-17 expression more effectively inhibits Notch pathway-mediated renal cancer cell proliferation and invasion. ADAM-17 may be a new target for future treatment of renal carcinoma.

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TÍTULO / TITLE: - Severe autoimmune hemolytic anemia with renal neoplasm.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Rhodes EC; Parikh SP; Bhattacharyya N

INSTITUCIÓN / INSTITUTION: - Department of Surgery, St. Joseph's Regional Medical Center, 703 Main Street, Paterson, NJ, 07503, USA, surgerystjoes@gmail.com.

RESUMEN / SUMMARY: - Autoimmune hemolytic anemia is a type of hemolytic anemia characterized by autoantibodies directed against red blood cells shortening their survival. When autoimmune hemolytic anemia is secondary to a paraneoplastic process, severe anemia can occur leading to significant morbidity and even mortality. Here we discuss the literature and present the case of a child with autoimmune hemolytic anemia from a paraneoplastic syndrome secondary to a renal tumor.

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TÍTULO / TITLE: Tissue fatty acid composition in human urothelial carcinoma.
RESUMEN / SUMMARY: Bladder cancer cells appear to have an altered lipid metabolism as evidenced by modulated lipogenic enzymes. The aim of this study is to investigate differences in tissue fat composition between malignant and adjacent normal urinary bladder tissue. Normal-appearing and malignant bladder tissues were collected from 31 patients with high-grade (Ta) urothelial carcinoma during transurethral resection (TUR). The fatty acid composition in the tissue was determined by gas liquid chromatography. In the bladder cancer tissue, levels of stearic acid (18:0; P = 0.01) and oleic acid (18:1n-9; P = 0.03) were higher, and the level of arachidonic acid (20:4n-6; P < 0.001) was lower than that in the normal-appearing bladder. Overall, bladder cancer tissue showed a significant reduction in total n-6 polyunsaturated fatty acid (-15.1%; P < 0.001). The change in the fatty acid composition may be regarded as an indicator of altered lipid metabolism occurring in vivo during human bladder tumourigenesis.

AUTORES / AUTHORS: Miryaghoubzadeh J; Darabi M; Madaen K; Shaaker M; Mehdizadeh A; Hajihosseini R
INSTITUCIÓN / INSTITUTION: Department of Biochemistry, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

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TÍTULO / TITLE: Pneumodissection: An Alternative Protective Technique for the Percutaneous Cryoablation of Small Renal Masses.
RESUMEN / SUMMARY: Introduction: Percutaneous cryoablation is an emerging treatment option for the small renal mass. It poses a risk of thermal injury to adjacent tissues, limiting its application. We describe pneumodissection, a novel technique for preventing thermal injury during percutaneous cryoablation. Materials and Methods: The cases of 4 patients who underwent percutaneous renal cryoablation and pneumodissection were retrospectively reviewed. Results: Pneumodissection mechanically separated four tumors from overlying bowel segments (mean distance 1.2 +/- 0.4 cm), permitting successful cryoablation. There were no complications or recurrences with 7.5 months of follow-up.
follow-up. Conclusions: Pneumodissection is a feasible displacement technique that facilitates percutaneous cryoablation in at-risk patients. Further study is warranted.

[778]
TÍTULO/TITLE: - Unusual Metastatic Sites From Renal Cell Carcinoma Detected by 18F-FDG PET/CT Scan.
RESUMEN/SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES/AUTHORS: - Aurangabadkar H; Ali Z
INSTITUCIÓN/INSTITUTION: - From the Department of Nuclear Medicine & PET/CT, Basavatarakam Indo-American Cancer Hospital & Research Institute, Hyderabad, India.
RESUMEN/SUMMARY: - Here we describe 2 cases of renal cell carcinoma where we found the unusual metastatic sites from renal cell carcinoma on F-FDG PET/CT scans in post-radical nephrectomy status. The first case resolves the venous migration of the tumor as a malignant thrombus arising from a remnant stump of the left renal vein, passing through hemiazygos vein further into the azygos vein and finally into the superior vena cava just before entering into the right atrium. The second case demonstrated extensive skeletal muscle deposits involving the muscles of the trunk as well as upper and lower extremities.

[779]
TÍTULO/TITLE: - Comparison of Fluid Absorption between Transurethral Enucleation and Transurethral Resection for Benign Prostate Hyperplasia.
RESUMEN/SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES/AUTHORS: - Ran L; He W; Zhu X; Zhou Q; Gou X
INSTITUCIÓN/INSTITUTION: - Department of Urology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China.
RESUMEN/SUMMARY: - Introduction: Although transurethral resection of prostate (TURP) remains the reference standard for benign prostate hyperplasia (BPH), the concern about complications promotes researchers to develop alternative surgical methods with fewer complications. In this study, we compared the safety and efficacy between the transurethral plasma kinetic enucleation of prostate (TUPKEP) and transurethral plasma kinetic resection of prostate (TUPKRP), mainly including absorption of irrigation fluid, the operation time, the weight of prostate tissue removed and severe complications. Methods:
Sixty BPH patients were randomly and evenly assigned to the TUPKEP or TUPKRP group. The irrigation fluid used in both groups was 1% ethanol-containing saline solution. The ethanol concentrations in the subjects’ end expiration were measured during operation. The volume of irrigation fluid absorbed was calculated accordingly. Results: No significant difference was found in operation time between two groups, whereas the weight of prostate tissue resection was significantly higher in the TUPKEP than that in the TUPKRP group. Conclusion: The study provides evidence for the safety, feasibility and effectiveness of both bipolar transurethral techniques. Further, compared to the TUPKRP group, the TUPKEP group has more efficient for resection of prostatic hyperplasia tissue, even though in terms of fluid absorption, no difference has been found in both groups. Ethanol monitoring is simple, safe and effective, which is beneficial for enhancing safety procedures.

[780]
TÍTULO / TITLE: - Adjuvant radiotherapy or early salvage radiotherapy in pT3R0 or pT3R1 prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Bartkowiak D; Bottke D; Wiegel T
INSTITUCIÓN / INSTITUTION: - Radiation Oncology Department, University Hospital Ulm, Ulm, Germany.
RESUMEN / SUMMARY: - PURPOSE OF REVIEW: As the appropriate management of patients after prostatectomy is still controversial, the two major approaches, adjuvant radiotherapy (ART) vs. prostate-specific antigen-based surveillance and - upon biochemical recurrence - salvage radiotherapy (SRT) are discussed. RECENT FINDINGS: Three prospectively randomized clinical trials into ART with 5-12 years median follow-up and overall 1800 patients show a significant gain in freedom from biochemical recurrence after prostatectomy and adjuvant irradiation (hazard ratio approximately 0.5). Only one study reported an improved overall survival (hazard ratio 0.72). Patients with pT3 and positive surgical margins are the most likely to profit from ART. Retrospective analyses of adjuvant vs. SRT suggest a similar oncological outcome if SRT is given early after recurrence, that is at a prostate-specific antigen of 0.5 ng/ml or less. Also, toxicity is similar with the two strategies. With positive lymph nodes, hormone therapy and optionally extended field radiotherapy can be recommended. SUMMARY: The alternative ART or surveillance along with SRT after prostatectomy cannot yet be decided on conclusively. Compliance, physical side-effects, psychological aspects and life expectancy should be taken into account when discussing treatment options.
Ongoing and planned trials will hopefully identify subgroups that profit most from one or the other strategy.

[781]

TÍTULO / TITLE: - Results of surgery for high-risk prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

Enlace al texto completo (gratuito o de pago)

AUTORES / AUTHORS: - Joniau S; Tosco L; Briganti A; Vanden Broeck T; Gontero P; Karnes RJ; Spahn M; Van Poppel H

INSTITUCIÓN / INSTITUTION: - aUrology, Department of Development and Regeneration, University Hospital of Leuven, Leuven, Belgium bDepartment of Urology, Vita-Salute San Raffaele Hospital, Milan, Italy cDepartment of Urology, University of Turin, Turin, Italy dDepartment of Urology, Mayo Clinic, Rochester, Minnesota, USA eDepartment of Urology, Inselspital, Bern, Switzerland *Both authors contributed equally to the manuscript.

RESUMEN / SUMMARY: - PURPOSE OF REVIEW: Surgery for high-risk prostate cancer (PCa) is applied frequently nowadays. Nevertheless, this approach is still surrounded by many controversies. The present review discusses the most recent literature regarding surgery for high-risk PCa. RECENT FINDINGS: As there is no standard definition of high-risk PCa, outcome comparison between series and treatment approaches is hampered. Nevertheless, recent radical prostatectomy series have shown excellent cancer-specific survival in patients with high-risk PCa. Even for very-high-risk PCa (cT3b-T4 or any cT, N1), surgery may be applied to highly selected patients as a first step of a multimodality approach. Recent experience with robot-assisted surgery opens new possibilities for a minimally invasive approach in this field. Patient selection for surgery was also addressed in recent studies. Excellent cancer-specific survival is seen when specimen-confined PCa is found at final histopathology; a recently published nomogram enables the prediction of specimen-confined disease. Another issue in high-risk PCa is the impact of age and comorbidities on cancer-specific and overall mortality. In a recent study, it was shown that patients with low comorbidity scores, even when at least 70 years old, had a significant risk of dying from their cancer and may benefit most from a surgical approach. A modified extended pelvic lymphadenectomy template was presented, providing optimal removal of positive lymph nodes. SUMMARY: Radical prostatectomy with extended pelvic lymphadenectomy delivers very good cancer-related outcomes in high-risk and very-high-risk PCa, often within a multimodal approach. Minimally invasive surgery and improved patient selection will be key to further improve oncological and functional outcomes.
[782]
**TÍTULO / TITLE:** Renal Cell Carcinoma Presenting as Isolated Deltoid Muscle Metastasis 12 Years After Radical Nephrectomy Detected on 18F-FDG PET/CT.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Bhoil A; Mittal BR; Bhattacharya A; Rane S; Nijhawan R; Gupta V

**INSTITUCIÓN / INSTITUTION:** From the *Department of Nuclear Medicine & PET, Cytology and Gynaecological Pathology and daggerGeneral Surgery, Postgraduate Institute of Medical Education and Research, Chandigarh 160 012, India.

**RESUMEN / SUMMARY:** We report a case of renal cell carcinoma detected to have isolated deltoid metastasis on F-FDG PET/CT 12 years after radical nephrectomy. Isolate muscle (deltoid) metastasis from renal cell carcinoma has not been reported in the literature.

[783]
**TÍTULO / TITLE:** Comparison of 18F Fluoride PET/CT and 99mTc-MDP Bone Scan in the Detection of Skeletal Metastases in Urinary Bladder Carcinoma.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Chakraborty D; Bhattacharya A; Mete UK; Mittal BR

**INSTITUCIÓN / INSTITUTION:** From the *Department of Nuclear Medicine; and daggerUrology, Postgraduate Institute of Medical Education & Research, Chandigarh, India.

**RESUMEN / SUMMARY:** AIM: The aim of this study was to compare F-fluoride PET/CT and Tc-MDP bone scintigraphy in the detection of skeletal metastases in urinary bladder carcinoma. PATIENTS AND METHODS: In this prospective study, 48 patients with urinary bladder carcinoma (44 male and 4 female patients, aged 35-80 years) underwent Tc-MDP planar and SPECT/CT bone scan (BS) followed by F-fluoride PET/CT within 48 hours. Skeletal metastasis diagnosed on each of these techniques was compared against a final diagnosis based on contrast-enhanced CT, MRI, skeletal survey, clinical follow-up, and histological correlation. RESULTS: F-fluoride PET/CT identified bony metastases and changed the management in 17 of 48 patients (35%). The sensitivity, specificity, positive predictive value, negative predictive value, and
accuracy of Tc-MDP planar BS were 82.35%, 64.51%, 56%, 86.95%, and 70.83%; of Tc-MDP SPECT/CT were 88.23%, 74.19%, 65.21%, 92%, and 79.16%; and of F-fluoride PET/CT were 100%, 87.09%, 80.95%, 100%, and 91.66%, respectively. Fair agreement between Tc-MDP planar BS and F-fluoride PET/CT (kappa = 0.42) and excellent agreement between SPECT/CT and F-fluoride PET/CT (kappa = 0.74) were found. CONCLUSIONS: F-fluoride PET/CT has higher sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in detecting bone metastases in urinary bladder carcinoma than conventional Tc-MDP planar BS. SPECT/CT improves all these parameters compared with planar BS and may serve as a cost-effective screening procedure for the detection of skeletal metastases in high-risk patients.

[784]

TÍTULO / TITLE: - Assessment of Screenees’ Knowledge on Prostate Cancer: Results of a Questionnaire Using the Fact Sheet.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Okihara K; Mikami K; Kamoi K; Kitamura K; Kawauchi A; Miki T
INSTITUCION / INSTITUTION: - Department of Urology, Kyoto Prefectural University of Medicine, Kyoto, Japan.
RESUMEN / SUMMARY: - Purpose: The aim of this study was to assess the screenees’ knowledge on prostate cancer and attitude to PSA screening using the Fact Sheet from one district, Kyoto, Japan. Methods: A PSA screening program is offered to people aged more than 54 years since 1995. The Fact Sheet consists of several chapters, as follows: (1) possibility of diagnosing prostate cancer in terms of the PSA threshold, and future morbidity risk, (2) benefit and harm of biopsy, (3) necessary examinations after the diagnosis of prostate cancer and risk for overdiagnosis and overtreatment, and (4) comorbidity of main treatments such as surgery and radiation therapy. Each screenee was asked how well the Fact Sheet was understood. Results: Of the 330 men, 288 read the Fact Sheet for the first time. Of those, 59 and 75% did not know that biopsy indication was determined based on the PSA value and the concept of overdiagnosis, respectively. Furthermore, 68% did not know that active surveillance is established as one option for prostate cancer treatment. However, the screenee’s knowledge in the 42 men who read the Fact Sheet previously improved substantially. Conclusions: The degree of comprehension of examinees is currently insufficient, and repeated enlightenment is required.
Laparoscopic versus Open Radical Cystectomy for Muscle-Invasive Bladder Cancer: A Single Institute Comparative Analysis.

Background: Open radical cystectomy (ORC) is the gold standard of treatment for muscle-invasive bladder cancer. Laparoscopic radical cystectomy (LRC) has emerged to provide an alternative. Methods: Between 2006 and 2012, 155 patients who underwent LRC or ORC were compared (mean follow-up 53 months). Results: The ORC group had shorter operative times (p < 0.0001), more blood loss (p < 0.00001), more transfusion requirement (p < 0.00001), longer postoperative length of hospital stay (p < 0.00001) and more morphine requirement (p = 0.02). No difference was found regarding lymph node yield (p = 0.07), positive margins (p = 0.11), cystectomy pathology results (p > 0.05) and positive lymph nodes (p = 0.02). The ORC group had less intraoperative complications (p = 0.03). No difference was found between the two groups regarding 5-year overall survival (p = 0.93), cancer-specific survival (p = 0.7) and recurrence-free survival (p = 0.62). Conclusion: LRC can be considered as an alternative to ORC with good operative and postoperative results in addition to comparable 5-year survival results.

Transitional Cell Carcinoma of the Ureteric Stump: A Systematic Review of the Literature.

Objective: To present a review of the literature using evidence-based criteria for diagnosis and treatment of malignant growths in the ureteric remnant following nephrectomy for non-malignant disease. Methods: A database search using the key search words was performed, producing a total of 16 articles published between 1952 and 2009. The Oxford Centre for Evidence-Based Medicine classification was used. Statistical significance was tested by Pearson correlation. Demographic data, reason for nephrectomy,
symptoms, time to diagnosis since initial nephrectomy, imaging modality and treatment option chosen, as well as histology and overall survival were reviewed. Results: Analysis was possible for 33 out of 63 cases reported in the literature. There was a male predominance (82%). Visible, painless haematuria was the presenting symptom in 72% of cases. Open ureterectomy was performed in the majority of patients (85%), while none had laparoscopic surgery. Transitional cell carcinoma was found in 66% of cases. Mean follow-up was 2.7 years. Metastases were detected in 36% and correlated significantly with cancer-specific mortality (95% CI: p < 0.001). Tumour stage, grade and cell type did not correlate significantly with mortality. Conclusion: Gross, painless haematuria is a feature highly suggestive of neoplastic change. Diagnosis often involves multimodality imaging and endoscopy. Complete ureterectomy with removal of bladder cuff, previously resected endoscopically, is the treatment of choice. Metastases at diagnosis and follow-up carry a worse prognosis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1177/1066896912475080
AUTORES / AUTHORS: - Singh G; Joshi P; Rao N; Seth A
INSTITUCIÓN / INSTITUTION: - 1All India Institute of Medical Sciences, New Delhi, India.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1136/postgradmedj-2012-200812rep
AUTORES / AUTHORS: - Wadhwa N; Jatawa SK; Tiwari A
INSTITUCIÓN / INSTITUTION: - School of Biotechnology, Rajiv Gandhi Proudyogiki Vishwavidyalaya, State Technological University of Madhya Pradesh, Airport Bypass Road, Bhopal 462033, Madhya Pradesh. wadhwanaha88@gmail.com.
RESUMEN / SUMMARY: - Bladder cancer is the fourth most frequently diagnosed malignant neoplasm and cause of cancer-related deaths in men and eighth in 583
women. Patients with bladder cancer undergo repeated cystoscopic examinations of the bladder to monitor for tumour recurrence which is invasive, costly and lacks accuracy. Therefore, the development of non-invasive urine based tests for the early detection of bladder cancer would be of tremendous benefit to both patients and healthcare systems. A number of urine based markers are available for the early diagnosis of bladder cancer. The diagnosis of bladder cancer relies on identifying malignant cells in the urine. All urinary markers have a higher sensitivity as compared with cytology but they score lower in specificity. Many soluble and cell based markers have been developed. Only two of the soluble and cell based markers have obtained the Food and Drug Administration approval. In the current review, the most recent literature of urinary markers is summarised. This article reports some of the more prominent urine markers and new technologies used nowadays.

[789]

TÍTULO / TITLE: - Dormancy in solid tumors: implications for prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ruppender NS; Morrissey C; Lange PH; Vessella RL
INSTITUCIÓN / INSTITUTION: - Department of Urology, University of Washington, Seattle, WA, USA.
RESUMEN / SUMMARY: - In cancer dormancy, residual tumor cells persist in a patient with no apparent clinical symptoms, only to potentially become clinically relevant at a later date. In prostate cancer (PCa), the primary tumor is often removed and many patients experience a prolonged period (>5 years) with no evidence of disease before recurrence. These characteristics make PCa an excellent candidate for the study of tumor cell dormancy. However, the mechanisms that constitute PCa dormancy have not been clearly defined. Additionally, the definition of tumor cell dormancy varies in the literature. Therefore, we have separated tumor cell dormancy in this review into three categories: (a) micrometastatic dormancy-a group of tumor cells that cannot increase in number due to a restrictive proliferation/apoptosis equilibrium. (b) Angiogenic dormancy-a group of tumor cells that cannot expand beyond the formation of a micrometastasis due to a lack of angiogenic potential. (c) Conditional dormancy-an individual cell or a very small number of cells that cannot proliferate without the appropriate cues from the microenvironment, but do not require angiogenesis to do so. This review aims to identify currently known markers, mechanisms, and models of tumor dormancy, in particular as they relate to PCa, and highlight current opportunities for advancement in our understanding of clinical cancer dormancy.
PURPOSE OF REVIEW: Concern for over and under-treatment of men with prostate cancer has led to an increased focus on the identification and selective treatment of men with high-risk features. The purpose of this review is to summarize the epidemiology, risk factors, and treatment trends of men with high-risk prostate cancer.

RECENT FINDINGS: Findings from recent trials on prostate-specific antigen-based screening suggest that screening has substantially reduced the incidence of high-risk prostate cancer. Men with high-risk disease tend to be older at diagnosis than those with low-risk disease. There is marked variation in the treatment of men with high-risk features; contemporary studies favor multimodal therapy, but high-risk disease is often under-treated with androgen deprivation alone, particularly among older men.

SUMMARY: Variations in the incidence, mortality, and treatment of men with high-risk prostate cancer may reflect heterogeneity among studies in the definition of high-risk disease. Future research should attempt to standardize definitions of high-risk prostate cancer to allow better comparison between studies and provide a more homogeneous assessment of natural history.
be established, rendering the discrimination of high-risk from nonhigh-risk patients a challenge. This review summarizes the contemporary definitions of high-risk prostate cancer and their clinical utility. RECENT FINDINGS: As currently defined, high-risk prostate cancer constitutes a heterogeneous group of tumors with varying pathological features and inconsistent outcomes. Some high-risk patients may harbor systemic disease and relapse after local definitive therapy, whereas a substantial proportion have localized cancers and may be cured by surgery alone. If properly identified, these high-risk patients should be deemed candidates for curative treatment and spared the morbidity of systemic therapy. Additional information derived from systematic prostate biopsy, magnetic resonance findings, and, possibly, pretreatment prostate-specific antigen kinetics may be incorporated into the currently available models to yield a better prediction and to allow more informed decision-making. SUMMARY: The quandary of how to define high-risk prostate cancer is pertinent. Various contemporary definitions of high-risk prostate cancer are available, most of which lack adequate sensitivity and specificity. Patients with high-risk clinically localized prostate cancer, by any of the current definitions, should not be uniformly disqualified from local definitive therapy with curative intent.

[792]
TÍTULO / TITLE: - Development of a label-free LC-MS/MS strategy to approach the identification of candidate protein biomarkers of disease recurrence in prostate cancer patients in a clinical trial of combined hormone and radiation therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Morrissey B; O’Shea C; Armstrong J; Rooney C; Staunton L; Sheehan M; Shannon A; Pennington SR
INSTITUCIÓN / INSTITUTION: - Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Belfield, Dublin, 4, Ireland.
RESUMEN / SUMMARY: - Prostate cancer is one of the leading causes of male mortality in the Western world. Currently, radiation combined with hormone treatment is one of the principle curative regimes for localised disease. Significantly, of the patients treated this way approximately 25% subsequently experience disease recurrence and may require further treatment. At present, prostate specific antigen (PSA) is used to monitor treatment and a rising serum PSA level can be indicative of treatment failure. However, PSA is relatively insensitive as both transient increases in PSA without disease recurrence and disease recurrence without a rise in PSA occur. Hence, more effective biomarkers to monitor treatment and predict disease recurrence are needed. In
this proof of principle study we used samples accrued under strict clinical trial governance and have applied a mass spectrometry based proteomic pipeline consisting of label free LC-MS biomarker discovery and multiple reaction monitoring confirmation strategy to identify a potential serum protein signature of disease recurrence. Ultimately, when extended and combined with validation studies using samples from other clinical trials we anticipate that this proteomics strategy will facilitate the development of a protein signature of significant clinical utility. This article is protected by copyright. All rights reserved.

[793]
TÍTULO / TITLE: - Estrogen receptor beta expression and androgen receptor phosphorylation correlate with a poor clinical outcome in hormone-naive prostate cancer and are elevated in castration-resistant disease.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Zellweger T; Sturm S; Rey S; Zlobec I; Gsponer JR; Rentsch CA; Terracciano LM; Bachmann A; Bubendorf L; Ruiz C
INSTITUCIÓN / INSTITUTION: - Department of Urology, St Claraspital, Basel, Switzerland Institute for Pathology, University Hospital Basel, University of Basel, Schonbeinstrasse 40, 4031 Basel, Switzerland Institute of Pathology, University of Bern, Bern, Switzerland Department of Urology, University Hospital Basel, Basel, Switzerland.
RESUMEN / SUMMARY: - Patients with advanced prostate cancer (PC) are usually treated with androgen withdrawal. While this therapy is initially effective, nearly all PCs become refractory to it. As hormone receptors play a crucial role in this process, we constructed a tissue microarray consisting of PC samples from 107 hormone-naive (HN) and 101 castration-resistant (CR) PC patients and analyzed the androgen receptor (AR) gene copy number and the protein expression profiles of AR, Serin210-phosphorylated AR (pAR(210)), estrogen receptor (ER)beta, ERalpha and the proliferation marker Ki67. The amplification of the AR gene was virtually restricted to CR PC and was significantly associated with increased AR protein expression (P<0.0001) and higher tumor cell proliferation (P=0.001). Strong AR expression was observed in a subgroup of HN PC patients with an adverse prognosis. In contrast, the absence of AR expression in CR PC was significantly associated with a poor overall survival. While pAR(210) was predominantly found in CR PC patients (P<0.0001), pAR(210) positivity was observed in a subgroup of HN PC patients with a poor survival (P<0.05). Epithelial ERalpha expression was restricted to CR PC cells (9%). ERbeta protein expression was found in 38% of both HN and CR PCs, but was elevated in matched CR PC specimens. Similar to pAR(210), the presence of ERbeta in HN patients was significantly associated with an adverse
prognosis (P<0.005). Our results strongly suggest a major role for pAR(210) and ERbeta in HN PC. The expression of these markers might be directly involved in CR tumor growth.

[794]
**TÍTULO / TITLE:** - Efficacy and Safety of Axitinib Versus Sorafenib in Metastatic Renal Cell Carcinoma: Subgroup Analysis of Japanese Patients from the Global Randomized Phase 3 AXIS Trial.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Ueda T; Uemura H; Tomita Y; Tsukamoto T; Kanayama H; Shinohara N; Tarazi J; Chen C; Kim S; Ozono S; Naito S; Akaza H

**INSTITUCIÓN / INSTITUTION:** - *Prostate Center and Division of Urology, Chiba Cancer Center, 666-2 Nitona-cho, Chuo-ku, Chiba-shi, Chiba 260-8717, Japan.  urolccc@yahoo.co.jp.

**RESUMEN / SUMMARY:** - OBJECTIVE: Axitinib is a potent and selective second-generation inhibitor of vascular endothelial growth factor receptors 1, 2 and 3. The efficacy and safety of axitinib in Japanese patients with metastatic renal cell carcinoma were evaluated. METHODS: A subgroup analysis was conducted in Japanese patients enrolled in the randomized Phase III trial of axitinib versus sorafenib after failure of one prior systemic therapy for metastatic renal cell carcinoma. RESULTS: Twenty-five (of 361) and 29 (of 362) patients randomized to the axitinib and sorafenib arms, respectively, were Japanese and included in this analysis. Median progression-free survival in Japanese patients was 12.1 months (95% confidence interval 8.6 to not estimable) for axitinib and 4.9 months (95% confidence interval 2.8-6.6) for sorafenib (hazard ratio 0.390; 95% confidence interval 0.130-1.173; stratified one-sided P = 0.0401). The objective response rate was 52.0% for axitinib and 3.4% for sorafenib (P = 0.0001). The common all-causality adverse events (all grades) in Japanese patients were dysphonia (68%), hypertension (64%), hand-foot syndrome (64%) and diarrhea (56%) for axitinib, and hand-foot syndrome (86%), hypertension (62%) and diarrhea (52%) for sorafenib. The safety profiles of axitinib and sorafenib in Japanese patients were generally similar to those observed in the overall population, with the exceptions of higher incidences of hypertension, dysphonia, hand-foot syndrome, hypothyroidism and stomatitis. CONCLUSIONS: Axitinib is efficacious and well tolerated in Japanese patients with previously treated metastatic renal cell carcinoma, consistent with the results in the overall population, providing a new targeted therapy for these Japanese patients.
[795] TÍTULO / TITLE: Can we decrease the acute proctitis in prostate cancer patients using hyaluronic acid during radiation therapy: a prospective historically controlled clinical study.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Cartei G
INSTITUCIÓN / INSTITUTION: International Academy of Environmental Sciences, Venice, Italy. giuseppecartei@iaes.info

[796] TÍTULO / TITLE: Evaluation of anatomic and morphologic nomogram to predict malignant and high-grade disease in a cohort of patients with small renal masses.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Bagrodia A; Harrow B; Liu ZW; Olweny EO; Faddegon S; Yin G; Tan YK; Han WK; Lotan Y; Margulis V; Cadeddu JA
INSTITUCIÓN / INSTITUTION: Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX.
RESUMEN / SUMMARY: OBJECTIVE: To evaluate a nomogram using the RENAL Nephrometry Score (RENA-L-NS) that was developed to characterize masses as benign vs. malignant and high vs. low grade in our patients with small renal masses treated with partial nephrectomy (PN). The nomogram was previously developed and validated in patients with widely variable tumor sizes. MATERIALS AND METHODS: Retrospective review of PN performed between 1/2003 and 7/2011. Imaging was reviewed by a urologic surgeon for RENAL-NS. Final pathology was used to classify tumors as benign or malignant and low (I/II) or high (III/IV) Fuhrman grade. Patient age, gender, and RENAL score were entered into the nomogram described by Kutikov et al. to determine probabilities of cancer and high-grade disease. Area under the curve was determined to assess agreement between observed and expected outcomes for prediction of benign vs. malignant disease and for prediction of high- vs. low-grade or benign disease. RESULTS: A total of 250 patients with 252 masses underwent PN during the study period; 179/250 (71.6%) had preoperative imaging available. RENAL-NS was assigned to 181 masses. Twenty-two percent of tumors were benign. Eighteen percent of tumors were high grade. Area under the curve was 0.648 for predicting benign vs. malignant disease and
0.955 for predicting low-grade or benign vs. high-grade disease. 

CONCLUSIONS: The RENAL-NS score nomogram by Kutikov does not discriminate well between benign and malignant disease for small renal masses. The nomogram may potentially be useful in identifying high-grade tumors. Further validation is required where the nomogram probability and final pathologic specimen are available.

[797]

**TÍTULO / TITLE:** - A randomised, wait-list controlled trial: evaluation of a cognitive-behavioural group intervention on psycho-sexual adjustment for men with localised prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Siddons HM; Wootten AC; Costello AJ

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Royal Melbourne Hospital, Parkville, Vic., Australia.

**RESUMEN / SUMMARY:** - OBJECTIVE: To examine the effectiveness of a cognitive-behavioural therapy (CBT) group intervention to facilitate improved psycho-sexual adjustment to treatment side effects in prostate cancer survivors post-radical prostatectomy. METHODS: A randomised, wait-list controlled trial was conducted with a total of 60 men who participated in a manualised 8-week cognitive-behavioural group intervention 6 months to 5 years post-radical prostatectomy for localised prostate cancer. Participants completed standardised questionnaires pre-intervention and post-intervention, which assessed mood state, stress, general and prostate cancer anxiety, quality of life and areas of sexual functioning. RESULTS: Paired samples t-tests identified a significant improvement in sexual confidence, masculine self-esteem, sexual drive/relationship and a significant decline in sexual behaviour from pre-intervention to post-intervention. Hierarchical regression analyses revealed that after controlling for covariates, participation in the group intervention significantly improved sexual confidence, sexual intimacy, masculine self-esteem and satisfaction with orgasm. CONCLUSIONS: This group-based CBT intervention for men post-radical prostatectomy for localised prostate cancer shows promising results in terms of improving quality of life. Copyright © 2013 John Wiley & Sons, Ltd.

[798]

**TÍTULO / TITLE:** - Antimitotic agents for the treatment of patients with metastatic castrate-resistant prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
INTRODUCTION: Metastatic castrate-resistant prostate cancer (mCRPC) is the second deadliest cancer in men. The group of taxanes, which target microtubules of mitotic cells, is currently the only chemotherapy which has proven to increase overall survival in mCRPC patients. Other mitotic inhibitors are being explored for their clinical potential in mCRPC treatment.

AREAS COVERED: In this review, we summarize recent developments in the application of mitotic inhibitors for mCRPC from a clinical perspective. The four main groups of mitotic inhibitors currently being tested in clinical trials are microtubule-inhibitors, polo-like kinase 1 inhibitors, aurora kinase inhibitors and kinesin-spindle protein inhibitors. Compounds of these groups of inhibitors that are in clinical development for mCRPC are discussed. For this extensive overview, relevant literature was searched in PubMed and retrieved from clinicaltrials.gov and presentations at ASCO/AACR meetings. EXPERT OPINION: In general, mitotic inhibitors are clinically well tolerated but exert limited antitumor activity compared to preclinical study results. However, efficacy of mitotic inhibitors is improving, either by personalizing treatment, by introducing more active compounds, by decreasing resistance of cancer cells against mitotic inhibitors or by using mitotic inhibitors in combination therapies.

[799]

Title: Expression analysis of MND1/GAJ, SPATA22, GAPDHS and ACR genes in testicular biopsies from non-obstructive azoospermia (NOA) patients.

BACKGROUND: High-throughput studies provide a wide spectrum of genes for use as predictive markers during testicular sperm...
extraction (TESE) in combination with ICSI. In this work, we used the specimens from testicular biopsies of men with non-obstructive azoospermia who underwent TESE to investigate the expression of spermatogenesis-related genes MND1, SPATA22, GAPDHS and ACR. METHODS: Testicular biopsy specimens were subdivided into three groups: hypospermatogenesis (HS); maturation arrest (MA); and Sertoli cell-only syndrome (SCO). The levels of expression of the spermatogenesis-related genes MND1, SPATA22, GAPDHS and ACR in the testes were compared among these three groups using the reverse transcription polymerase chain reaction (RT-PCR) technique. RESULTS: Analysis of the expression of spermatogenic genes in human testes with abnormal spermatogenesis showed different expression patterns in patients from different groups. Fertilization rate for studied set of patients was 66% and pregnancy rate 29%. For HS group fertilization rate was 72% and pregnancy rate 32%, while for MA group fertilization and pregnancy rates were 54% and 26%, respectively. Fertilization rates in relation to the studied genes were uniformly around 70%, pregnancy rates for ACR and GAPDHS genes were surprisingly low at 6% and 8% correspondingly. CONCLUSIONS: Analysis of the expression of genes involved in spermatogenesis can be a fast additional test for the level of spermatogenesis in testicular samples.

TÍTULO / TITLE: - Assessment of antimicrobial prophylaxis to prevent perioperative infection in patients undergoing prostate brachytherapy: multicenter cohort study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Taoka R; Togo Y; Kubo T; Kido M; Miki K; Kiyota H; Egawa S; Sugawara T; Yasuda M; Nakano M; Deguchi T; Nishino M; Ishikawa K; Shiromukuma R; Matsumoto M; Shigemura K; Tanaka K; Arakawa S; Fujisawa M; Wada K; Watanabe T; Kumon H; Kobayashi K; Matsubara A; Sho T; Hamasuna R; Matsumoto T; Hayami H; Nakagawa M; Yamamoto S
INSTITUCIÓN / INSTITUTION: - Department of Urology, Hyogo College of Medicine, 1-1 Mukogawa-cho, Nishinomiya, Hyogo, 663-8501, Japan, rikiya0910@yahoo.co.jp.
RESUMEN / SUMMARY: - To propose an appropriate prophylactic antimicrobial therapy for patients undergoing brachytherapy, we evaluated the relationships between various antimicrobial prophylaxis (AMP) protocols and the incidence of postimplant infections in a multicenter cohort study conducted in Japan. The records of 826 patients with localized prostate cancer who underwent a transperineal 125I brachytherapy procedure between January 2009 and
December 2010 were retrospectively reviewed. Perioperative infections, including surgical site and remote infections, were recorded up to postoperative day 30. A total of 6 (0.73 %) patients had a perioperative infection following seed implantation, of whom all received AMP for 1 or more days. None of the patients who received a single-dose protocol of AMP using fluoroquinolone p.o. or penicillin with a beta-lactamase inhibitor i.v. developed a perioperative infection. Statistical analysis showed that a single-dose protocol was more significantly related to a lower risk of perioperative infection as compared to the other AMP protocols examined (p = 0.045). Furthermore, our results indicated that bacteriuria and preoperative hair removal were risk factors of perioperative infection with statistical significance (p = 0.007, p = 0.004). Analysis of patient clinical parameters, including age, American Society of Anesthesiologists score, diabetes mellitus, prostate volume, numbers of implanted seeds and needle punctures, operation time, and indwelling duration time of the Foley catheter, did not reveal significant differences in terms of perioperative infection. Our results indicated that a single-dose AMP protocol is sufficient to prevent perioperative infections following seed implantation. On the other hand, AMP is only one of several measures to prevent perioperative infectious complications. It is necessary to know that the patient must have no bacteriuria and that preoperative hair removal should be avoided.
reported. RESULTS: No adverse reactions to anti-3-18F-FACBC PET/CT were noted. On a patient basis, 11C-choline PET/CT was positive in 3 patients and negative in 12 (detection rate 20 %), and anti-3-18F-FACBC PET/CT was positive in 6 patients and negative in 9 (detection rate 40 %). On a lesion basis, 11C-choline detected 6 lesions (4 bone, 1 lymph node, 1 local relapse), and anti-3-18F-FACBC detected 11 lesions (5 bone, 5 lymph node, 1 local relapse). All 11C-choline-positive lesions were also identified by anti-3-18F-FACBC PET/CT. The TBR of anti-3-18F-FACBC was greater than that of 11C-choline in 8/11 lesions, as were image quality and contrast. CONCLUSION: Our preliminary results indicate that anti-3-18F-FACBC may be superior to 11C-choline for the identification of disease recurrence in the setting of biochemical failure. Further studies are required to assess efficacy of anti-3-18F-FACBC in a larger series of prostate cancer patients.

[802]

TÍTULO / TITLE: - Prognostic impact of preoperative hematological disorders and a risk stratification model in bladder cancer patients treated with radical cystectomy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Sejima T; Morizane S; Yao A; Isoyama T; Saito M; Amisaki T; Koumi T; Takenaka A

INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Surgery, Tottori University Faculty of Medicine, Yonago, Japan.

RESUMEN / SUMMARY: - OBJECTIVES: The present study investigated prognostic indicators, including clinicopathological and preoperative hematological factors, and developed a prognostic factor-based risk stratification model in bladder cancer patients treated with radical cystectomy. METHODS: Data were collected from 249 consecutive bladder cancer patients treated with radical cystectomy without neoadjuvant therapy. Prognostic values of the preoperative hematological parameters, along with the patients' clinicopathological parameters were evaluated. A risk stratification model was developed to predict disease-specific survival after radical cystectomy using the regression coefficients of multivariate analysis. RESULTS: In the multivariate analysis, preoperative hemoglobin and C-reactive protein levels, as well as the pathological factors of T stage, positive surgical margin and lymph node metastasis, were independently predictive of disease-specific survival. Low hemoglobin (<10.5 g/dL), a high C-reactive protein (>0.5 mg/dL), extravesical T stage (>/>=pT3a) and positive surgical margin were independent predictors of poor disease-specific survival. The risk stratification model showed significant differences in disease-specific survival between the three
subgroups. CONCLUSIONS: This is the first report to show the significance of combining preoperative hemoglobin with the pathology of radical cystectomy specimens as an independent predictor for disease-specific survival, and it also represents the largest contemporary series to date demonstrating that two types of preoperative hematological disorders, assessed by hemoglobin and C-reactive protein, are independent predictors in bladder cancer patients treated with radical cystectomy. Our risk stratification model could provide physicians with useful prognostic information for identifying patients who might be candidates for multimodal treatments.

[803]

**TÍTULO / TITLE:** - Nephronectin Expression in Glomeruli of Renal Biopsy Specimens from Various Kidney Diseases: Nephronectin Is Expressed in the Mesangial Matrix Expansion of Diabetic Nephropathy.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Nephron Clin Pract. 2013 May 8;122(3-4):114-121.

**AUTORES / AUTHORS:** - Nakatani S; Ishimura E; Mori K; Fukumoto S; Yamano S; Wei M; Emoto M; Wanibuchi H; Inaba M

**INSTITUCIÓN / INSTITUTION:** - Department of Metabolism, Endocrinology and Molecular Medicine, Osaka City University Graduate School of Medicine, Osaka, Japan.

**RESUMEN / SUMMARY:** - Background: In a previous proteomic study, we detected increased expression of nephronectin in the glomeruli from patients with diabetic nephropathy (DN). The aim of the present study was to clarify the usefulness of determining glomerular expression of nephronectin in kidney disease. Methods: We performed immunohistochemical staining for nephronectin in renal biopsy specimens from patients with a variety of kidney diseases (n = 190). The percentage of nephronectin-positive areas in the glomeruli was analyzed using an image analyzer. Results: Nephronectin immunoreactivity was clearly, strongly positive in the mesangial expansion and nodular lesions of DN (n = 18), whereas nephronectin immunoreactivity was negative in IgA glomerulonephritis, membranoproliferative glomerulonephritis, lupus nephritis, membranous glomerulonephritis, minor glomerular abnormalities, crescentic glomerulonephritis, and other kidney diseases, such as amyloidosis and light chain deposition disease. Nephronectin was stained weakly in sclerotic lesions, such as focal segmental glomerulosclerosis and hypertensive nephropathy. The percentage of nephronectin-positive areas in the glomeruli from DN patients [15.1 +/- 4.7% (n = 18)] was significantly higher than that for other kidney diseases [5.5 +/- 3.6% (n = 172)] (p < 0.001). In multiple regression analyses, fasting plasma glucose and hemoglobin A1c were significantly associated with the increase in the percentage of nephronectin-
positive areas in the glomeruli (beta = 0.23, p < 0.001 and beta = 0.16, p = 0.045, respectively). Conclusions: The expression of nephronectin was sufficient to discriminate DN from other kidney diseases with mesangial matrix expansion and nodular lesions. We consider that nephronectin staining could be helpful in the diagnosis of DN.

[804]
TÍTULO / TITLE: - Effect of the timing of orchiectomy on survival in patients with metastatic germ cell tumors of testis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Fedyanin M; Tryakin A; Bulanov A; Fainshtein I; Zakharova T; Matveev V; Garin A; Tjulandin S
INSTITUCIÓN / INSTITUTION: - Department of Clinical Pharmacology & Chemotherapy, N. N. Blokhin Russian Cancer Research Center, Moscow, Russia. Electronic address: fedianinmu@mail.ru.
RESUMEN / SUMMARY: - OBJECTIVES: Classically, orchiectomy (OE) is the first step of treatment in patients with metastatic germ cell tumors (mGCTs) of testis. However, some patients have severe symptoms of disease, which require immediate beginning of chemotherapy (CT) followed by OE. This retrospective analysis was performed to find the effect of time constraints of delayed OE on survival in patients with mGCT. METHODS AND MATERIALS: We analyzed the data of 1,483 CT-naive patients with advanced mGCT of the testis treated in our Department from 1986 to 2009. Delayed OE was performed on 71 (4.8%) patients: seminoma in 8 patients (11.2%), nonseminomatous tumor in 50 patients (70.4%), and unknown tumor histology in 13 patients (18.4%). Twenty percent, 40%, and 40% of patients belonged to good, intermediate, and poor International Germ Cell Cancer Consensus Group prognostic groups, respectively. Median time from the beginning of the CT to OE was 18 (range, 1-250) days. OE was performed on 39 (55%), 21 (29.5%), and 11 (15.5%) patients during cycle 1, cycle 2 to completion of CT, and after the finishing of induction CT, respectively. Median follow-up time was 156 (range, 3-241) months. Etoposide and cisplatin-based CTs were received by 66 patients (93%). RESULTS: Three-year overall survival (OS) of all 1,483 patients was 75%. An excellent primary tumor response to CT was observed among the patients, who had delayed OE after completion of CT (n = 11): only mature teratoma (n = 4) and tumor necrosis (n = 7) were found. The 3-year OS in patients with delayed OE was 63%. OE performed after completion of CT was associated with better prognosis. The 3-year OS in patients with delayed OE
performed during the cycle 1 (group 1) was 67%, cycle 2 to completion of CT (group 2) was 39%, and after finishing of CT (group 3) was 88% (groups 1 vs. 3: hazard ratio 3.7, 95% confidence interval 0.69-10.1, P = 0.15; groups 2 vs. 3: P = 0.01, hazard ratio 8.1, 95% confidence interval 1.32-18.72). It seems that if OE had been performed during CT, the beginning of the successive cycle was delayed and dose intensity of CT was decreased. CONCLUSIONS: In case of severe symptoms of disease, which require an immediate start of CT, performing OE simultaneously with other surgeries after completion of induction CT was associated with better OS, when compared with performing OE during induction CT.

TÍTULO / TITLE: - Use of a Clinical Assistant to Screen Patients With Genitourinary Cancer to Encourage Entry into Clinical Trials and Use of Supportive Medication: A Pilot Project at a Canadian Cancer Center.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Lun G; Atenafu EG; Knox JJ; Sridhar SS; Tannock IF; Joshua AM
INSTITUCIÓN / INSTITUTION: - School of Medicine, Queen’s University.
RESUMEN / SUMMARY: - BACKGROUND: The central goal of cancer care is to improve patient outcomes through advancing medical knowledge. Therefore, participation in clinical trials is encouraged to demonstrate efficacy and understand toxicities of medical interventions. In the oncology setting, these interventions are also frequently accompanied by clinical care to maintain bone health throughout the course of disease. In this study we examined the use of a study screener to enhance accrual and highlight bone health issues in a tertiary referral cancer center. PATIENTS AND METHODS: A study screener was introduced into 4 separate genitourinary clinics in a tertiary referral cancer center. Over a retrospective and subsequent prospective 10-week period, clinical trial accrual and bone health parameters were measured. RESULTS: There were no statistically significant differences between the retrospective and prospective periods in probability of approaching a patient for clinical trials (P = .60), accrual rates (P = .80), or proportion of patients later found ineligible (P = .31). The difference in initiation of calcium and vitamin D between the retrospective and prospective patients was statistically significant (P < .0001) and the difference between cohorts for starting treatment with zoledronic acid or denosumab was statistically significant (P = .02) and approached significance for the prostate cancer patients (P = .12). CONCLUSION: This pilot study suggests that in an academic setting, there is appropriate physician awareness
of clinical trial availability, however the use of medication to improve bone health is suboptimal, and requires further research to identify and remove barriers to appropriate use including additional evidence of beneficial toxicity-benefit and cost-benefit ratios.
INTRODUCTION: A kidney tumor is an abnormal growth within the kidney that usually occurs over a period of a time. Each tumor has its own characteristics and it is important to know what tumor the patient has so that the proper treatment can be administered. Kidney tumors can be benign or malignant. Symptoms of all types of kidney tumors are very similar and unspecific. The aims of study: a) To determine how many patients, who were clinically and radiologically diagnosed with kidney tumor, after surgical intervention, have histopathologically confirmed renal cell carcinoma; b) To compare number of female and male patients have histopathologically confirmed renal cell carcinoma; c) To compare numbers of patients with renal cell carcinoma who are older than 50 years with the ones who are younger than 50 years; d) To determine the most common risk factors for renal cell carcinoma; e) To determine the most common symptoms of renal cell carcinoma; f) To determine what was the most common stage of kidney cancer in the time when it was histopathologically confirmed. MATERIAL AND METHODS: This study was observational, descriptive, retrospective study of renal cell carcinoma. The study consisted of 28 patients who were clinically and radiologically diagnosed with kidney tumor, which was surgically removed and histopathologically tested. All patients were surgically treated at the Urological Clinic of Clinical Centre University of Sarajevo from 1/1/2012 to 06/30/2012. RESULTS: from 28 patients with a kidney tumor 26 had RCC, the most of patients with RCC were older than 50 years (22 patients), there was 7 female and 19 male patients, the most common symptom was pain (10 patients), the most common risk factor, excluding age, was hypertension (11 patients), patients with RCC was usually diagnosed stage 4 Fuhrman (11 patients). CONCLUSION: Doctors should give their intention to discover early symptoms of renal cell carcinoma and to do preventive exams and tests in the population of patients who have one or more risk factors for developing this disease. Early diagnose and appropriate therapy could reduce mortality and morbidity of the patients with renal cell carcinoma, and could also reduce costs of treatment.
Prostate cancer (PCA) is the second most common tumour in men worldwide. Whereas prostate specific antigen (PSA) is an established biochemical marker, the optimal imaging method for all clinical scenarios has not yet been found. With the rising number of PET centres there is an increasing availability and use of 18F-/11C-choline or 11C-acetate for staging of PCA. However, to date no final conclusion has been reached as to whether acetate or choline tracers should be preferred. In this review we provide an overview of the performance of choline and acetate PET for staging the primary and recurrent disease and lymph nodes in PCA, based on the literature of the last 10 years. Although predominantly choline has been used rather than acetate, both tracers performed in a similar manner in published studies. Choline as well as acetate have insufficient diagnostic accuracy for the staging of the primary tumour, due to a minimum detectable tumour size of 5 mm and inability to differentiate PCA from benign prostate hyperplasia, chronic prostatitis and high-grade intraepithelial neoplasia. Regarding lymph node staging, choline tracers have demonstrated a high specificity. Unfortunately, the sensitivity is only moderate. For staging recurrent disease, sensitivity depends on the level of serum PSA (PSA should be >2 ng/ml). This applies to both choline and acetate. However, despite these limitations, a significant number of patients with recurrent disease can benefit from PET imaging by a change in treatment planning.
RESUMEN / SUMMARY: - PURPOSE: Our previous retrospective study reported that bladder neck involvement (BNI), as well as tumor grade and stage, was a significant risk factor for progression in primary non-muscle invasive bladder cancer (NMIBC). We prospectively validated BNI as a significant predictor for progression using a new cohort of patients with primary NMIBC. PATIENTS AND METHODS: A total of 297 new Japanese patients who underwent transurethral resection and were pathologically diagnosed with Ta or T1 urothelial carcinoma were enrolled in this prospective study. Clinicopathologic data were collected at study entry. Multivariate Cox proportional hazards regression models were performed to identify the independent predictors for progression. A predictive scoring model for progression was developed using the regression coefficients (RCs) from the final multivariate model. The predictive ability of the model was assessed using Harrell's c-index. RESULTS: With a median follow-up of 37 months, 16 patients (5.4%) progressed. Progression probability at 1 and 5 years were 1.5% and 8.0%, respectively. Multivariate analysis revealed that histologic grade 3 (hazard ratio [HR] 9.45, P = 0.0004, RC 2.25), pathologic T1 stage (HR 6.91, P = 0.0014, RC 1.93), and BNI (HR 11.75, P = 0.0009, RC 2.46) were all independent predictors of progression. When all 3 variables were scored as 1 point and the patients were divided into 3 groups, progression rates were clearly discriminated (P<0.0001). The c-index was 0.80. CONCLUSIONS: This prospective validation study has shown that BNI is a significant prognostic factor for progression in primary NMIBC. The scoring model including BNI enables the physician to classify patients with primary NMIBC into 3 groups with clearly different progression rates.

[810]
TÍTULO / TITLE: - Comment on: EGFR mutational status in Brazilian patients with penile carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - da Silva AM; Lisboa BC; Cunha IW; Rocha RM; Zequi SC; Guimaraes GC; Vassallo J; Soares FA
INSTITUCIÓN / INSTITUTION: - A. C. Camargo Cancer Center, CIPE - International Research and Teaching Center for Cancer , Rua Tagua, #440, Liberdade - 01508-010 - Sao Paulo-SP , Brazil +55 11 21895185 ; licemuglia@yahoo.com.br.
RESUMEN / SUMMARY: - The authors describe the results on EGFR molecular alterations of 29 Brazilian patients with penile carcinoma (PC). DNA extracted from frozen tumor tissue of all patients was submitted to direct sequencing of
the four exons (18 - 21) responsible for the EGFR tyrosine-kinase activity. Corroborating the data by Di Lorenzo et al. published in Expert Opin Ther Targets, none of the sequenced tumor samples showed relevant alterations in the four studied exons of the EGFR gene.

[811]
TÍTULO / TITLE: - The role of intracrine androgen metabolism, androgen receptor and apoptosis in the survival and recurrence of prostate cancer during androgen deprivation therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Fiandalo MV; Wu W; Mohler JL
INSTITUCIÓN / INSTITUTION: - Department of Urology, Roswell Park Cancer Institute, Buffalo, NY 14263, USA.
RESUMEN / SUMMARY: - Prostate cancer (CaP) is the most frequently diagnosed cancer and leading cause of cancer death in American men. Almost all men present with advanced CaP and some men who fail potentially curative therapy are treated with androgen deprivation therapy (ADT). ADT is not curative and CaP recurs as the lethal phenotype. The goal of this review is to apply our current understanding of CaP and castration-recurrent CaP (CR-CaP) to earlier studies that characterized ADT and the molecular mechanisms that facilitate the transition from androgen-stimulated CaP to CR-CaP. Reexamination of earlier studies also may provide a better understanding of how more newly recognized mechanisms, such as intracrine metabolism, may be involved with the early events that allow CaP survival after initiation of ADT and subsequent development of CR-CaP.

[812]
TÍTULO / TITLE: - Improved therapeutic targeting of the androgen receptor: rational drug design improves survival in castration-resistant prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Lim AC; Attard G
INSTITUCIÓN / INSTITUTION: - Section of Medicine, The Institute of Cancer Research, Sutton, Surrey, SM2 5NG, United Kingdom.
RESUMEN / SUMMARY: - The growth and dependence of Prostate Cancer (PCa) on androgen stimulation led to the use of castration to reduce circulating levels of androgens and anti-androgens to directly target the androgen receptor (AR) ligand-binding domain (LBD). However, castration-resistant prostate cancer (CRPC) resistant to anti-androgens invariably develops and can be associated with AR genomic aberrations (mutations, amplification) and/or an increase in
AR mRNA expression. Efforts to more effectively target the AR in CRPC led to the rational design of CYP17A1 inhibitors and more potent antiandrogens. The front-runner 2nd generation rationally-designed therapeutics targeting the AR, abiraterone and enzalutamide have been shown to improve survival and clinical outcome for CRPC patients. Several other CYP17A1 inhibitors and antiandrogens are in clinical and preclinical development. However, patients ultimately progress and current evidence suggests that this can occur through reactivation of AR signaling. Several ongoing programs aim to develop LBD independent therapeutic strategies that for example target the N terminus domain (NTD) of the AR or chaperone proteins. Rationally-designed approaches combining different strategies for targeting the AR or associated pathways also warrant clinical evaluation.

[813]

**TITULO / TITLE:** Prognostic implication of infiltrative growth pattern and establishment of novel risk stratification model for survival in patients with upper urinary tract urothelial carcinoma.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** Int J Clin Oncol. 2013 Apr 3.

**AUTORES / AUTHORS:** Hashimoto T; Nakashima J; Inoue R; Gondo T; Ohno Y; Tachibana M

**INSTITUCIÓN / INSTITUTION:** Department of Urology, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo, 160-0023, Japan, ha-tkc@tokyo-med.ac.jp.

**RESUMEN / SUMMARY:** PURPOSE: To investigate the prognostic significance of infiltrative growth pattern (INF) and to develop a novel risk stratification model for disease-specific survival (DSS) in patients with upper urinary tract urothelial carcinoma (UTUC). METHODS: This study included 113 patients with UTUC treated with radical nephroureterectomy. Pathological features, including INF, were compared with DSS. INF was classified into 3 patterns (INFa, INFb, and INFc). The prognostic factors of DSS were evaluated with univariate and multivariate Cox proportional hazard model analyses. A risk stratification model based on the relative risks of DSS was then established. RESULT: Univariate analysis revealed that patients with high-grade tumor, pathological T stage >/=T3, a non-expanding infiltration pattern (INF >/=b), sessile-type carcinoma, the presence of lymphovascular invasion and positive lymph node involvement showed significantly lower survival rates than their respective counterparts. In the multivariate analysis, high grade tumor, positive lymph node involvement and INF >/=b were independent predictors for DSS (p < 0.05). The patients were stratified into 3 risk groups. The 5-year DSS rates were 94.4 % in the low-
risk group, 67.5% in the intermediate-risk group and 20.5% in the high-risk group. CONCLUSION: In addition to lymph node involvement and pathological tumor grade, INF is a novel independent prognostic factor in patients with UTUC treated with radical nephroureterectomy. Our risk stratification model developed using these 3 factors may help clinicians identify patients with a poor prognosis who might be good candidates for clinical trials of innovative therapies.

[814]
TÍTULO / TITLE: - Human Anti-Macrophage Migration Inhibitory Factor (MIF) Antibodies Inhibit Growth of Human Prostate Cancer Cells In Vitro and In Vivo.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hussain F; Freissmuth M; Volkel D; Thiele M; Douillard P; Antoine G; Thurner P; Ehrlich H; Schwarz HP; Scheiflinger F; Kerschbaumer RJ
INSTITUCIÓN / INSTITUTION: - 1Institute of Pharmacology, Center of Physiology and Pharmacology, Medical University of Vienna.
RESUMEN / SUMMARY: - Macrophage migration inhibitory factor (MIF) is a proinflammatory cytokine, originally discovered for its eponymous effect and now known for pleiotropic biological properties in immunology and oncology. Circulating MIF levels are elevated in several types of human cancer including prostate cancer. MIF is released presumably by both, stromal and tumor cells and enhances malignant growth and metastasis by diverse mechanisms, such as stimulating tumor cell proliferation, suppressing apoptotic death, facilitating invasion of the extracellular matrix and promoting angiogenesis. Recently described fully human anti-MIF antibodies were tested in vitro and in vivo for their ability to influence growth rate and invasion of the human PC3 prostate cancer cell line. In vitro, the selected candidate antibodies BaxG03, BaxB01 and BaxM159 reduced cell growth and viability by inhibiting MIF-induced phosphorylation of the central kinases p44/42 mitogen-activated protein kinase (ERK1/2) and protein kinase B (AKT). Incubation of cells in the presence of the antibodies also promoted activation of caspases 3/7. The antibodies furthermore inhibited MIF-promoted invasion and chemotaxis as transmigration through matrigel along a MIF gradient was impaired. In vivo, pharmacokinetic parameters (half-life, volume of distribution and bioavailability) of the antibodies were determined and a proof of concept was obtained in a PC3-xenograft mouse model. Treatment with human anti-MIF antibodies blunted xenograft tumor growth in a dose-dependent manner. We therefore conclude that the anti-
MIF antibodies described neutralize some of the key tumor promoting activities of MIF and thus limit tumor growth in vivo.
TÍTULO / TITLE: - Incremental costs of prostate cancer trials: Are clinical trials really a burden on a public payer system?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Jones B; Syme R; Eliasziw M; Eigl BJ
INSTITUCIÓN / INSTITUTION: - Research Assistant, Alberta Health Services, Alberta Clinical Cancer Research Unit, Tom Baker Cancer Centre, Calgary, AB;
RESUMEN / SUMMARY: - INTRODUCTION: Clinical trials are a critical component of improving cancer prevention and treatment strategies. However, the perception that patients enrolled in trials consume more resources than those receiving the standard-of-care (SOC) has contributed to an increasingly research-averse environment. Current economic data pertaining to the per-patient costs of prostate cancer trials relative to SOC treatment are limited. METHODS: A retrospective observational cohort study was conducted to compare costs incurred by 59 prostate cancer patients participating in a mix of industry and non-industry sponsored clinical trials with costs incurred by an equal number of eligible non-participants who received SOC over a year. Resource utilization was tracked and quantified to standardized price templates. RESULTS: No difference in overall resource utilization was seen between trial and SOC patients (two-tailed t-test, n = 118, p = 0.99). Variability in the types of resources used by each group indicated that, while trial patients may take up significantly more clinic time (p = 0.001) and undergo more tests and procedures (p = 0.001), SOC patients are more likely to receive other costly interventions, such as radiation therapy (p < 0.001). Other variables (e.g., pathology, diagnostic imaging, prescribed therapies) were statistically indistinguishable between groups. CONCLUSION: This study revealed differences in the cost distribution of patients enrolled in clinical trials versus those receiving SOC, which could be used to improve resource allocation. The lack of evidence for a difference in overall cost provides an argument for payers to more fully support clinical research without fear of adverse financial consequences. Further analysis is required.

[817]
TÍTULO / TITLE: - Identification of Prostate Cancer-Associated MicroRNAs in Circulation Using a Mouse Model of Disease.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Selth LA; Townley SL; Gillis JL; Tilley WD; Butler LM
RESUMEN / SUMMARY: - MicroRNAs (miRNAs) derived from the cell-free fractions of blood are emerging as useful noninvasive markers of cancer. However, many tumors display significant molecular heterogeneity, which is likely to be reflected in the circulating miRNA fingerprints associated with that pathology. One strategy to minimize such heterogeneity is to employ genetically engineered mouse models of human cancer. Here, we describe a method to profile miRNAs in the serum of a mouse model of prostate cancer, TRansgenic Adenocarcinoma of Mouse Prostate (TRAMP), and discuss practical considerations for translating these potential biomarkers into a clinical setting.

[818] 
TÍTULO / TITLE: - Twenty-three-year review of disease patterns from renal biopsies: an experience from a pediatric renal center. 
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary 
AUTORES / AUTHORS: - Yin XL; Zou MS; Zhang Y; Wang J; Liu TL; Tang JH; Qiu LR; Chen Y; Yuan HQ; Zhou JH 
INSTITUCIÓN / INSTITUTION: - Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei Province - PR China. 
RESUMEN / SUMMARY: - Background: The aim of this study was to investigate the clinical and pathological characteristics as well as their associations with trends for diseases in 1,579 pediatric renal biopsies from 1989 to 2012. Methods: The clinical and pathological data were retrospectively analyzed for children undergoing renal biopsy from 1989 to 2012 in our hospital. Results: Primary glomerulonephritis (PGN) accounted for 60.1% of total cases, followed by secondary glomerulonephritis (SGN) (31.2%) and hereditary nephropathy (8.3%). The major clinical patterns of PGN and SGN were nephritic syndrome (NS) and Henoch-Schönlein purpura nephritis (HSPN), respectively. Minimal change disease/mild disease (MCD/ML), IgAN and mesangial proliferative glomerulonephritis (MsPGN) were the most common pathological patterns of PGN. Male patients were most likely to suffer from NS, HBV-associated glomerulonephritis (HBVGN) or Alport syndrome, while females were most likely to suffer from isolated hematuria, rapidly progressive glomerulonephritis (RPGN), lupus nephritis (LN), ANCA-associated glomerulonephritis or thin basement membrane disease. The proportions of NS, isolated hematuria, acute nephritic syndrome, chronic nephritic syndrome, HBVGN, LN and hemolytic uremic syndrome changed significantly with aging. The clinical patterns of PGN were significantly correlated with the distribution of pathological types: MCD/ML
and IgMN presented most often as NS; MCD/ML and IgAN presented most often as isolated hematuria; IgAN and MsPGN presented most often as hematuria with proteinuria. The spectrum of NS, HSPN, HBVGN and IgAN changed during the 23 years, and the percentage of repeated renal biopsies was low (1.2%) in pediatric cases with kidney disease. Conclusions: Glomerular diseases in children are closely related to age and sex of patient. The spectrum of kidney diseases from our center has changed significantly over the last 23 years.

[819]

**TÍTULO / TITLE:** - High-Dose Bevacizumab in the Treatment of Patients With Advanced Clear Cell Renal Carcinoma: A Phase II Trial of the Sarah Cannon Oncology Research Consortium.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Hainsworth JD; Shipley DL; Reeves J Jr; Arrowsmith ER; Barnes EK; Waterhouse DM

**INSTITUCIÓN / INSTITUTION:** - Sarah Cannon Research Institute, Nashville, TN; Tennessee Oncology, PLLC, Nashville, TN. Electronic address: aso@scresearch.net.

**RESUMEN / SUMMARY:** - BACKGROUND: The dose of bevacizumab necessary to optimally inhibit tumor angiogenesis in advanced renal cell carcinoma is unknown. In this phase II trial, we evaluated the efficacy and safety of 2 escalated doses of bevacizumab in patients with advanced clear cell renal carcinoma. PATIENTS AND METHODS: Eligible patients had metastatic or locally advanced unresectable clear cell renal carcinoma. Patients who were previously untreated or who had previously received vascular endothelial growth factor receptor (VEGFR)-targeted therapy were eligible and were considered separately in the efficacy evaluation. Two doses of bevacizumab were evaluated in sequential cohorts: 15 mg/kg every 2 weeks and 15 mg/kg weekly. The initial reevaluation was at 8 weeks; responding and stable patients continued treatment, with reevaluations every 8 weeks until tumor progression or unacceptable toxicity occurred. RESULTS: One hundred nineteen eligible patients were enrolled and received bevacizumab 15 mg/kg every 2 weeks (n = 61) or bevacizumab 15 mg/kg weekly (n = 58). Seventy patients were previously untreated with VEGFR-targeted therapy. In previously untreated patients, the overall response rate was 19%, with a median progression-free survival (PFS) of 7.8 months. Less activity was seen in patients previously treated with VEGFR-targeted agents (overall response rate, 4%; median PFS, 3.7 months). There was no suggestion of any difference in efficacy between the
2 dose levels tested. Both dose levels were tolerated well by most patients, with a spectrum of toxicity typical for bevacizumab. Grade ¼ proteinuria was more frequent with both of these escalated doses, particularly with 15 mg/kg weekly. CONCLUSION: Although administration of escalated doses of bevacizumab was feasible in patients with advanced clear cell renal carcinoma, there was no suggestion that these doses were more efficacious than bevacizumab administered at the standard dose of 10 mg/kg every 2 weeks.

[TITULO / TITLE: Pazopanib as Second-Line Treatment After Sunitinib or Bevacizumab in Patients With Advanced Renal Cell Carcinoma: A Sarah Cannon Oncology Research Consortium Phase II Trial.

RESUMEN / SUMMARY: BACKGROUND: This phase II trial examined the activity and toxicity of second-line treatment with pazopanib after failure of first-line single-agent treatment with sunitinib or bevacizumab in patients with advanced clear cell renal carcinoma. PATIENTS AND METHODS: Fifty-five patients with metastatic clear cell renal carcinoma who had previously received first-line treatment with sunitinib (39 patients) or bevacizumab (16 patients) were enrolled. Patients received pazopanib 800 mg orally daily and were evaluated for response after 8 weeks of treatment. Responses were measured using Response Evaluation Criteria in Solid Tumors (RECIST), version 1.0, and confirmed with repeated scans after 8 weeks. Patients with objective response or stable disease continued treatment until disease progression or unacceptable toxicity occurred. RESULTS: Fifteen of 55 patients (27%) had objective response to pazopanib. An additional 27 patients (49%) had stable disease, for a disease control rate of 76%. After a median follow-up of 16.7 months, the median progression-free survival for the entire group was 7.5 months (95% confidence interval, 5.4-9.4 months). Similar progression-free survival was observed regardless of whether previous treatment was with sunitinib or bevacizumab. The estimated overall survival rate for the entire group at 24 months was 43%. CONCLUSION: Pazopanib is an active agent for the treatment of advanced clear cell renal carcinoma, even after failure of sunitinib or bevacizumab. Treatment with pazopanib should be considered early in the sequence of therapy for patients with advanced renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Bjerklund Johansen TE; Witzsch U; Greene D
INSTITUCIÓN / INSTITUTION: - Urology Department, Aarhus University Hospital, 8200 Aarhus, Denmark. tebj@ki.au.dk.
RESUMEN / SUMMARY: - Radiotherapy is the main salvage option after primary radical prostatectomy. Radical prostatectomy, cryosurgical ablation and high-intensity focused ultrasound are the main salvage options after primary radiotherapy. After primary radiotherapy, long-term oncological outcome of salvage radical prostatectomy and salvage cryosurgical ablation is fairly comparable with the results of primary radical prostatectomy and primary cryosurgical ablation. Side effects of salvage radical prostatectomy in elite centers are acceptable and side effects of salvage cryosurgical ablation in tertiary centers are almost the same as after primary cryosurgical ablation. Good long-term data after salvage high-intensity focused ultrasound are lacking and the risk of side effects is considerable. After primary radical prostatectomy, there is a high level of evidence for oncological benefit of salvage radiotherapy. Careful patient selection is important for all salvage modalities.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Lin J; Whalen M; Holder D; Hruby G; Decastro GJ; McKiernan J
INSTITUCIÓN / INSTITUTION: - Columbia University College of Physicians and Surgeons, New York, New York, USA.
RESUMEN / SUMMARY: - INTRODUCTION: We examined the effects of neoadjuvant chemotherapy (NC) in the treatment of muscle invasive urothelial carcinoma of the bladder in those with mixed histology (MH) versus those with pure urothelial carcinoma (UC). MATERIALS AND METHODS: Between 2000-2012, 195 patients were identified with clinical stage T2-T4, N0-Nx, M0-Mx UCB who had either NC (+/- radical cystectomy) (n = 63) or radical cystectomy (RC) alone (n = 132). Tumors were classified as either pure UC or MH. Endpoints included downstaging to pT0 and overall survival. Multivariable Cox regression and the Kaplan-Meier method were used to estimate the effects of
histological type and treatment given on overall mortality. RESULTS: The rate of downstaging to pT0 was higher in NC treated patients with both MH (p = 0.048) and pure UC (p < 0.0001), as compared to those in each group who did not receive NC. NC was not a significant predictor of overall survival for MH patients in a Cox multivariate model (p = 0.54). However, among all patients treated with NC, MH was found to be a predictor of poorer survival compared to UC (p = 0.02). CONCLUSIONS: Prior evidence on the benefits of NC for patients with MH is mixed, but our data suggests that there is improvement in rate of pT0 on final pathology in those treated with NC, regardless of histology. Although patients with MH fare worse than those with pure UC in the setting of NC, given the significantly higher rate of pT0 at final pathology, strong consideration should be given to use of NC in the treatment of MH muscle invasive bladder cancer patients.

[823]
TÍTULO / TITLE: - Bone Morphogenetic Protein-6 Induces Castration Resistance in Prostate Cancer Cells through Tumor Infiltrating Macrophages.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Lee GT; Jung YS; Ha Y; Kim JH; Kim WJ; Kim IY
INSTITUCIÓN / INSTITUTION: - Section of Urologic Oncology and Dean and Betty Gallo Prostate Cancer Center, The Cancer Institute of New Jersey and Robert Wood Johnson Medical School, New Brunswick, NJ, 08901.
RESUMEN / SUMMARY: - Bone morphogenetic protein (BMP) is a pleiotropic growth factor that has been implicated in inflammation and prostate cancer (CaP) progression. In the present study, we have investigated the potential role of BMP-6 in the context of macrophages and castration-resistant prostate cancer. When the androgen-responsive murine (TrampC1 and PTENCaP8) and human (LNCaP) CaP cell lines were co-cultured with macrophages in the presence of dihydrotestosterone, BMP-6 increased androgen-responsive promoter activity and cell count significantly. Subsequent studies revealed that BMP-6 increased the expression level of androgen receptor (AR) mRNA and protein in CaP cell lines only in the presence of macrophages. Simultaneously, the AR antagonists bicalutamide and MDV3100 partially or completely blocked BMP-6-induced macrophage-mediated androgen hypersensitivity in CaP cells. Abolishing interleukin-6 (IL-6) signaling with neutralizing antibody in CaP/macrophages co-culture inhibited the BMP-6-mediated AR upregulation in CaP cells. Using TrampC1 and PTENCaP8 cells with a tetracycline-inducible expression of BMP-6, the induction of BMP-6 in vivo resulted in a significant resistance to castration. This resistance though, was blocked upon the removal of macrophages with clodronate-liposomes. Taken together, these results
demonstrate that BMP-6 induces castration resistance by increasing the expression of AR through the macrophage-derived IL-6. This article is protected by copyright. All rights reserved.

[824]

TÍTULO / TITLE: Targeting the Vav3 oncogene enhances docetaxel-induced apoptosis through the inhibition of androgen receptor phosphorylation in LNCaP prostate cancer cells under chronic hypoxia.
RESUMEN / SUMMARY: Background: The Vav family of Rho/Rac guanosine nucleotide exchange factors comprises three members in mammalian cells. Vav3 enhances androgen receptor (AR) activity during progression to androgen independence in prostate cancer. We examined Vav3 small interfering RNA (siRNA) effects on cell proliferation and apoptosis in docetaxel-treated LNCaP cells under chronic hypoxia (LNCaPH). METHODS: We examined individual and combined effects of Vav3 siRNA (si-Vav3) and docetaxel on cell growth and apoptosis under chronic hypoxia by cell proliferation, flow cytometric, DNA fragmentation, and immunoblot analyses. To clarify the molecular basis of si-Vav3- and docetaxel-induced apoptosis, we analyzed alterations in phosphatidylinositol 3-kinase (PI3K)/Akt, extracellular signal-regulate kinase (ERK), c-jun N-terminal kinase (JNK), and AR pathways using kinase inhibitors in LNCaPH cells. The effects of si-Vav3/atelocollagen complex alone or in combination with docetaxel were assessed on xenografts in nude mice by tumor growth delay. RESULTS: Vav3 overexpression was observed in LNCaPH compared with the expression under normoxia. Interrupting Vav3 signaling using siRNA enhanced docetaxel-induced cell growth suppression compared with that induced by docetaxel alone by inhibition of Akt and ERK phosphorylation, resulting in AR phosphorylation inhibition. In addition to increased B-cell lymphoma 2 (Bcl-2) phosphorylation through JNK signaling in response to docetaxel, si-Vav3 enhanced docetaxel-induced apoptosis, as characterized by the accumulation of sub-G1 phase cells and DNA fragmentation, through Bcl-xL/Bcl-2-associated death promoter (Bad) dephosphorylation, resulting in increased caspase-9, caspase-3, and cleaved poly(ADP-ribose) polymerase activation. Xenograft tumor growth was slightly
inhibited by si-Vav3/atelocollagen complex injection and combined use of si-Vav3/atelocollagen complex and docetaxel produced a greater effect than docetaxel alone. CONCLUSIONS: Interrupting Vav3 signaling enhances docetaxel-induced apoptosis in LNCaP cells under chronic hypoxia by inhibiting the PI3K/Akt, ERK, and AR signaling pathways. Therapy targeting Vav3 in combination with docetaxel may have practical implications for managing castration-resistant prostate cancer.

[825]

TÍTULO / TITLE: - Multiple therapeutic peptide vaccines consisting of combined novel cancer testis antigens and anti-angiogenic peptides for patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Suzuki H; Fukuhara M; Yamaura T; Mutoh S; Okabe N; Yaginuma H; Hasegawa T; Yonechi A; Osugi J; Hoshino M; Kimura T; Higuchi M; Shio Y; Ise K; Takeda K; Gotoh M

RESUMEN / SUMMARY: - BACKGROUND: Vaccine treatment using multiple peptides derived from multiple proteins is considered to be a promising option for cancer immune therapy, but scientific evidence supporting the therapeutic efficacy of multiple peptides is limited. METHODS: We conducted phase I trials using a mixture of multiple therapeutic peptide vaccines to evaluate their safety, immunogenicity and clinical response in patients with advanced/recurrent NSCLC. We administered two different combinations of four HLA-A24-restricted peptides. Two were peptides derived from vascular endothelial growth factor receptor 1 (VEGFR1) and 2 (VEGFR2), and the third was a peptide derived from up-regulated lung cancer 10 (URLC10, which is also called lymphocyte antigen 6 complex locus K [LY6K]). The fourth peptide used was derived from TTK protein kinase (TTK) or cell division associated 1 (CDCA1). Vaccines were administered weekly by subcutaneous injection into the axillary region of patients with montanide ISA-51 incomplete Freund’s adjuvant, until the disease was judged to have progressed or patients requested to be withdrawn from the trial. Immunological responses were primarily evaluated using an IFN-gamma ELiSPOT assay. RESULTS: Vaccinations were well tolerated with no severe treatment-associated adverse events except for the reactions that occurred at the injection sites. Peptide-specific T cell responses against at least one peptide were observed in 13 of the 15 patients enrolled. Although no patient exhibited complete or partial responses, seven patients (47%) had stable disease for at least 2 months. The median overall survival time was 398 days, and the 1- and 2-year survival rates were 58.3% and 32.8%, respectively. CONCLUSION: Peptide vaccine therapy using a mixture of four novel peptides
was found to be safe, and is expected to induce strong specific T cell responses. Trial registration: These studies were registered with ClinicalTrials.gov NCT00633724 and NCT00874588.

TÍTULO / TITLE: - Clinical applications of multiparametric MRI within the prostate cancer diagnostic pathway.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Dickinson L; Ahmed HU; Allen C; Barentsz JO; Carey B; Futterer JJ; Heijmink SW; Hoskin P; Kirkham AP; Padhani AR; Raj Persad ChM; van der Meulen J; Villers A; Emberton M
INSTITUCIÓN / INSTITUTION: - Division of Surgery and Interventional Sciences, University College London, Gower Street London, UK.

TÍTULO / TITLE: - The cost-effectiveness of blue light cystoscopy in bladder cancer detection: United States projections based on clinical data showing 4.5 years of follow up after a single hexaminolevulinate hydrochloride instillation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Garfield SS; Gavaghan MB; Armstrong SO; Jones JS
INSTITUCIÓN / INSTITUTION: - GfK Bridgehead, Wayland, Massachusetts, USA.
RESUMEN / SUMMARY: - INTRODUCTION: Several studies, including the recently published phase III study by Stenzl and colleagues have demonstrated that hexaminolevulinate hydrochloride, when used with blue light fluorescence cystoscopy, improves detection of non-muscle invasive bladder tumors compared to white light cystoscopy and transurethral resection of bladder tumors (TURB) alone. MATERIALS AND METHODS: The objective of this study was to conduct a detailed assessment of the cost-effectiveness of using hexaminolevulinate hydrochloride with blue light cystoscopy as an adjunct to white light versus white light cystoscopy alone at time of initial TURB in the United States. A probabilistic decision tree model, using TreeAge Pro 2011 software, was developed using base case scenario cost and utility estimates. RESULTS: Incorporation of hexaminolevulinate hydrochloride into diagnostic cystoscopy results in lower costs over 5 years ($25,921) as compared to those patients who initially receive white light cystoscopy ($30,581). Those patients who initially receive hexaminolevulinate hydrochloride blue light TURB also experience a lower overall cancer burden. CONCLUSIONS: Hexaminolevulinate hydrochloride may be cost effective when used at first
TURB for patients with suspected new or recurrent non-muscle invasive bladder cancer.

[828]
TÍTULO / TITLE: - Fibroblast Growth Factor Receptor 3 is a Rational Therapeutic Target in Bladder Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
    ●●Enlace al texto completo (gratuito o de pago) 1158/1535-7163.MCT-12-1150
AUTORES / AUTHORS: - Gust KM; McConkey DJ; Awrey S; Hegarty PK; Qing J; Bondaruk J; Ashkenazi A; Czerniak B; Dinney CP; Black PC
INSTITUCIÓN / INSTITUTION: - 1Vancouver Prostate Centre, Department of Urologic Sciences, University of British Columbia.
RESUMEN / SUMMARY: - Activating mutations of Fibroblast growth factor receptor-3 (FGFR3) have been described in approximately 75% of low-grade papillary bladder tumors. In muscle invasive disease, FGFR3 mutations are found in 20% of tumors, but overexpression of FGFR3 is observed in about half of cases. Therefore, FGFR3 is a particularly promising target for therapy in bladder cancer. Up to now most drugs tested for inhibition of FGFR3 have been small molecule, multi-tyrosine kinase inhibitors. More recently, a specific inhibitory monoclonal antibody targeting FGFR3 (R3Mab) has been described and tested pre-clinically. In this study, we have evaluated mutation and expression status of FGFR3 in 19 urothelial cancer cell lines and a cohort of 170 American bladder cancer patients. We demonstrated inhibitory activity of R3Mab on tumor growth and corresponding cell signaling in three different orthotopic xenografts of bladder cancer. Our results provide the pre-clinical proof of principle necessary to translate FGFR3 inhibition with R3Mab into clinical trials in patients with bladder cancer.

[829]
TÍTULO / TITLE: - Recurrent gene fusions in prostate cancer: their clinical implications and uses.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
    ●●Enlace al texto completo (gratuito o de pago) 1007/s11934-013-0321-1
AUTORES / AUTHORS: - Hessels D; Schalken JA
RESUMEN / SUMMARY: - Gene fusions, resulting from chromosomal rearrangements, have been attributed to leukaemias and soft tissue sarcomas. The recent discovery of a recurrent gene fusion TMPRSS2-ERG in approximately half of the prostate cancers tested indicates that gene fusions also play a role in the onset of common epithelial cancers. Prostate cancer is the most commonly diagnosed malignancy and the second leading cause of cancer-related deaths in the Western male population. It is a heterogeneous disease, both in terms of pathology and clinical presentation. Since the discovery of the TMPRSS2-ERG fusion, other gene fusions have been reported, most of which result in the androgen-regulated over-expression of the oncogene ERG or other ETS transcription factors. The high prevalence of these gene fusions represents a distinct class of tumours, which may give more insight in the heterogeneity of the disease. These gene fusions are of interest as biomarkers for diagnosis of prostate cancer, and some of them could be useful in predicting the presence of aggressive disease. This review focuses on the biological significance and clinical implementation of gene fusions, and particularly the most commonly reported TMPRSS2-ERG fusion, in prostate cancer.

[830]

TÍTULO / TITLE: - Renal function adaptation up to the fifth decade after treatment of children with unilateral renal tumor: A cross-sectional and longitudinal study.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Cozzi DA; Ceccanti S; Frediani S; Mele E; Cozzi F

INSTITUCIÓN / INSTITUTION: - Paediatric Surgery Unit, Sapienza University of Rome, Azienda Policlinico Umberto I, Rome, Italy.

RESUMEN / SUMMARY: - BACKGROUND: Mild-to-moderate renal function loss may be an independent risk factor for cardiovascular disease and overall mortality. As in adults with renal carcinoma nephrectomy is associated with a high risk for moderate renal function loss, we aimed to assess the renal function adaptation over a long period of time in children with unilateral renal tumor (URT). PROCEDURE: Seventy-two children who underwent surgery for URT were enrolled in this study. Glomerular filtration rate was estimated (eGFR) with the Modification of Diet in Renal Study or the Schwartz equation, as appropriate for the age. RESULTS: Twelve patients treated by nephron-sparing surgery (Group A) and 42 treated by nephrectomy (Group B) had an age between 2 and 30 years; 18 patients treated by nephrectomy had an age between 33 and 51 years (Group C). At cross-sectional follow-up 8% patients of Group A, 42% of Group B and 78% of Group C presented a mild-to-moderate
renal function. The longitudinal data stratified by post-operative intervals showed that patients of Group C presented a significant progressive decrease in mean +/- standard deviation eGFR (88.1 +/- 22.6 during the third decade after surgery vs. 66.6 +/- 15.6 ml/min/1.73 m² during the fifth decade after surgery; P = 0.02). The longitudinal data stratified by age showed that patients with an age between 45 and 54 years presented a mean eGFR significantly lower than that expected for the physiological renal function decline with aging (P = 0.001). CONCLUSION: Aging is associated with a mild-to-moderate renal function loss in many adult patients following nephrectomy during childhood for URT.

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[831]
TÍTULO / TITLE: - Editorial Comment from Dr Miki to Risk factors for chronic kidney disease after chemotherapy for testicular cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Miki T
INSTITUCIÓN / INSTITUTION: - Department of Urology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan.
tmiki@koto.kpu-m.ac.jp.

[832]
TÍTULO / TITLE: - MRI-Guided Biopsy for Prostate Cancer Detection: A Systematic Review of Current Clinical Results.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Overduin CG; Futterer JJ; Barentsz JO
INSTITUCIÓN / INSTITUTION: - Department of Radiology, Radboud University Nijmegen Medical Centre, Geert Grootplein Zuid 10, P.O. Box 9101 (766), 6500 HB, Nijmegen, the Netherlands, c.overduin@rad.umcn.nl.
RESUMEN / SUMMARY: - In-bore magnetic resonance-guided biopsy (MRGB) has been increasingly used in clinical practice to detect prostate cancer (PCa). This review summarizes the current clinical results of this biopsy method. A systematic literature search was performed in the PubMed and Embase databases. Of 2,035 identified records, 49 required full review. In all, ten unique studies reporting clinical results of MRGB could be included. Reported PCa detection rates ranged from 8 to 59 % (median 42 %). The majority of tumors
detected by MRGB were clinically significant (81-93 %). Most frequent complications of MRGB are transient hematuria (1-24 %) and short-term perirectal bleeding (11-17 %). Major complications are rare. Based on the reviewed literature, MRGB can be regarded an accurate and safe diagnostic tool to detect clinically significant PCa. However, as general availability is limited, this procedure should be reserved for specific patients. Appropriate indications will have to be determined.

[833]
**TÍTULO / TITLE:** - Androgen receptor and prostate cancer: new insights in an old target translate into novel therapeutic strategies.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](enlace-al-resumen)
**REVISTA / JOURNAL:** - Curr Drug Targets. 2013 Apr;14(4):399-400.
**AUTORES / AUTHORS:** - Heemers HV

[834]
**TÍTULO / TITLE:** - Clinical analysis of the PADUA and the RENAL scoring systems for renal neoplasms: A retrospective study of 245 patients undergoing laparoscopic partial nephrectomy.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](enlace-al-resumen)
**AUTORES / AUTHORS:** - Zhang ZY; Tang Q; Li XS; Zhang Q; Mayer WA; Wu JY; Yang XD; Zhang XC; Wang XY; Zhou LQ
**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Peking University First Hospital, Institute of Urology, Peking University, National Urological Cancer Center.
**RESUMEN / SUMMARY:** - OBJECTIVE: To investigate the clinical significance of preoperative aspects and dimensions used for anatomic (PADUA) and radius exophytic/endophytic nearness anterior/posterior location (RENA L) scoring systems for renal neoplasms in patients undergoing laparoscopic partial nephrectomy. METHODS: A retrospective analysis was carried out on clinical data of 245 Chinese patients with renal neoplasms undergoing laparoscopic partial nephrectomy from June 2008 to June 2012. The perioperative complications and variables, as well as PADUA and RENAL score, were compared. RESULTS: The PADUA and RENAL scoring systems were significantly associated with percent change in estimated glomerular filtration rate (P = 0.032 and P = 0.026 respectively), whereas the RENAL scoring system was also significantly associated with warm ischemia time (P = 0.032). On multivariate analysis, both scores were able to predict percent change in estimated glomerular filtration rate (PADUA, P = 0.011; RENAL, P = 0.028).
There were no significant associations between the two scoring systems assessed and the occurrence of complications or tumor stage. The correlation between PADUA classification and RENAL nephrometry score was significant (P < 0.0001). Fleiss’ generalized kappa was 0.69-0.89 for the various components of the PADUA score and 0.67-0.89 for the RENAL nephrometry components. CONCLUSIONS: The PADUA classification and RENAL nephrometry score are comprehensive assessment tools for delineating renal tumor anatomy. The reproducibility of the PADUA and RENAL scores is substantial, but further research is required to evaluate its performance in more accurately predicting operative and patient-related outcomes.
Prostate cancer is one of the most prevalent cancers in males and ranks as the second most common cause of cancer-related deaths. 2-methoxyestradiol (2-ME), an endogenous estrogen metabolite, is a promising anticancer agent for various types of cancers. Although 2-ME has been shown to activate c-Jun-NH2-kinase (JNK) and mitochondrial-dependent apoptotic signaling pathways, the underlying mechanisms, including downstream effectors, remain unclear. Here, we report that the human Bcl-2 homology 3 (BH3)-only protein harakiri (Hrk) is a critical effector of 2-ME-induced JNK/mitochondria-dependent apoptosis in prostate cancer cells. Hrk mRNA and protein are preferentially upregulated by 2-ME, and Hrk induction is dependent on the JNK activation of c-Jun. Hrk knockdown prevents 2-ME-mediated apoptosis by attenuating the decrease in mitochondrial membrane potential, subsequent cytochrome c (cyt c) release, and caspase activation. Involvement of the proapoptotic protein Bak in this process suggested the possible interaction between Hrk and Bak. Thus, Hrk activation by 2-ME or its overexpression displaced Bak from the complex with antiapoptotic protein Bcl-xL, whereas deletion of the Hrk BH3 domain abolished its interaction with Bcl-xL, reducing the proapoptotic function of Hrk. Finally, Hrk is also involved in the 2-ME-mediated reduction of X-linked inhibitor of apoptosis through Bak activation in prostate cancer cells. Together, our findings suggest that induction of the BH3-only protein Hrk is a critical step in 2-ME activation of the JNK-induced apoptotic pathway, targeting mitochondria by liberating proapoptotic protein Bak. Mol Cancer Ther; 12(6); 1-11. ©2013 AACR.

Proton Beam Radiation Therapy for Prostate Cancer - Is the Hype (and the Cost) Justified?

Although in use for over 40 years, proton beam therapy for prostate cancer has only recently come under public scrutiny, due to its
increased cost compared to other forms of treatment. While the last decade has seen a rapid accumulation of evidence to suggest that proton beam therapy is both safe and effective in this disease site, a rigorous comparison to other radiotherapy techniques has not yet been completed. In this review, we provide an in-depth look at the evidence both supporting and questioning proton beam therapy’s future role in the treatment of prostate cancer, with emphasis on its history, physical properties, comparative clinical and cost effectiveness, advances in its delivery and future promise.

[839]

**Título / Title:** Coordinate patterns of estrogen receptor, progesterone receptor, and Wilms tumor 1 expression in the histopathologic distinction of ovarian from endometrial serous adenocarcinomas.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary


**Autores / Authors:** Fadare O; James S; Desouki MM; Khabele D

**Institución / Institution:** Department of Pathology, Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN, USA; Department of Obstetrics and Gynecology, Vanderbilt University School of Medicine, Nashville, TN, USA. Electronic address: oluwolefadare@yahoo.com

**Resumen / Summary:** The purpose of this study is to assess whether composite or coordinate immunoexpression patterns of estrogen receptor (ER), progesterone receptor (PR), and Wilms tumor 1 (WT1) gene can significantly distinguish between endometrial serous carcinoma (ESC) and ovarian serous carcinoma (OSC). Immunohistochemical analyses were performed on whole tissue sections from 22 uterus-confined ESCs and on a tissue microarray of 140 high-grade, pan-stage OSCs, using antibodies to ER, PR, and WT-1. Estrogen receptor, PR, and WT1 expressions were present in 37%, 49%, and 81% of OSC, respectively, but these markers were also present in 18%, 27%, and 36% of ESC. The ER+/PR+/WT1+ coordinate profile was identified in 33.6% of OSC but in none of ESC (P = .0006), resulting in a calculated sensitivity and specificity of this profile for OSC of 33.6% and 100%, respectively. By contrast, the ER-/PR-/WT1- coordinate profile was identified in 41% of ESC but in only 6.4% of OSC (P = .0001), resulting in a calculated sensitivity and specificity of this profile for ESC of 50% and 94%. In summary, in the differential diagnosis between OSC and ESC, positivity for all 3 markers favors an extrauterine origin, whereas negativity for all 3 markers is supportive of an endometrial origin. The use of single markers for this purpose is not recommended, as each lacks
optimal discriminatory power. Coordinate profiles, in general, have a high specificity but low sensitivity in this differential diagnosis.

[840]
TÍTULO / TITLE: - Prognostic potential of ERG (ETS-related gene) expression in prostatic adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Szasz AM; Majoros A; Rosen P; Srivastava S; Dobi A; Szendroi A; Kulka J; Nyirady P
INSTITUCIÓN / INSTITUTION: - 2nd Department of Pathology, Semmelweis University, 93 Ulloi ut, 1091, Budapest, Hungary, cac@korb2.sote.hu.
RESUMEN / SUMMARY: - PURPOSE: Following patients after prostatectomy can be expensive and stressful, therefore, a novel and reliable approach to improve stratification is needed both at diagnosis of PCa and following its treatment. We evaluate the association of both ERG and claudin-4, claudin-5, and beta-catenin expression in tumor tissues of patients with organ-confined and advanced prostatic adenocarcinomas. METHODS: A total of 30 patients were included in the study. Nine men who underwent radical prostatectomy for organ-confined (pT2N0M0) cancer (OCC), 10 patients with clinically advanced cancer (CAC), and 11 controls with benign prostatic hypertrophy (BPH). Using immunohistochemistry applied to tissue microarrays, each group was evaluated for beta-catenin, claudin-4, claudin-5, and ERG expression. RESULTS: The expression of ERG was higher in the CAC group when compared to OCC and BPH (p = 0.7684, p = 0.0224, respectively). Among these patients, 5 from the CAC (45 %) and 5 from the OCC group (56 %) stained positively for ERG (p = 1.0). The mean staining score for those with ERG+ advanced cancer was greater than that for the ERG+ organ-confined cancer (p = 0.0209). ERG staining correlated with Gleason score (Pearson’s correlation: 0.498, p = 0.0051), but not with serum PSA level (Pearson’s correlation: 0.404, p = 0.1202). When analyzing outcome data, high ERG expressing tumors have shown a significantly worse overall survival (p = 0.0084). CONCLUSIONS: Our results of presence or absence of claudin-4 and claudin-5 and ERG staining intensities suggest their potential as prognostic factors for prostate cancer.

[841]
TÍTULO / TITLE: - Kinetics of testosterone recovery in clinically localized prostate cancer patients treated with radical prostatectomy and subsequent short-term adjuvant androgen deprivation therapy.
Androgen deprivation therapy (ADT) is a standard treatment for metastatic, recurrent and locally advanced prostate cancer (PCa). The aim of this study is to investigate the timing and extent of testosterone recovery in clinically localized PCa patients treated with radical prostatectomy (RP) and subsequent short-term adjuvant ADT. A total of 95 localized PCa patients underwent RP and 9-month adjuvant ADT were included in this prospective study. Serum testosterone level was measured before adjuvant ADT, at ADT cessation, and at 1, 3, 6, 9 and 12 months after cessation of ADT. A Cox proportional hazards model was used to assess variables associated with the time of testosterone normalization. The results showed that median patient age was 67 years and median testosterone level before adjuvant ADT was 361 (230-905) ng dl⁻¹. All patients finished 9-month adjuvant ADT and achieved castrate testosterone level. At 3 months after ADT cessation, testosterone recovered to supracastrate level in 97.9% patients and to normal level in 36.9% patients. The percentage of patients who recovered to normal testosterone level increased to 66.3%, 86.3% and 92.6% at 6, 9 and 12 months, respectively. Cox regression model found that higher baseline testosterone level (>/=300 ng dl⁻¹) was the only variable associated with a shorter time to testosterone normalization (hazard ratio: 1.98; P = 0.012). In conclusion, in most patients, testosterone recovered to supracastrate level at 3 months and to normal level at 12 months after 9-month adjuvant ADT cessation. Patients with higher baseline testosterone level need shorter time of testosterone normalization.


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Zhou C; Zhao XM; Li XF; Wang C; Zhang XT; Liu XZ; Ding XF; Xiang SL; Zhang J

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Key Laboratory of Protein Chemistry and Developmental Biology, Ministry of Education of China, College of Life Science, Hunan Normal University, Changsha 410081, China.

RESUMEN / SUMMARY: - Aim: To investigate the effects of curcumin on proliferation and apoptosis in testicular cancer cells in vitro and to investigate its molecular mechanisms of action. Methods: NTera-2 human malignant testicular germ cell line and F9 mouse teratocarcinoma stem cell line were used. The anti-proliferative effect was examined using MTT and colony formation assays. Hoechst 33258 staining, TUNEL and Annexin V-FITC/PI staining assays were used to analyze cell apoptosis. Protein expression was examined with Western blot analysis and immunocytochemical staining. Results: Curcumin (5, 10 and 15 mumol/L) inhibited the viability of NTera-2 cells in dose- and time-dependent manners. Curcumin significantly inhibited the colony formation in both NTera-2 and F9 cells. Curcumin dose-dependently induced apoptosis of NTera-2 cells by reducing FasL expression and Bcl-2-to-Bax ratio, and activating caspase-9, -8 and -3. Furthermore, curcumin dose-dependently reduced the expression of AP transcription factor AP-2gamma in NTera-2 cells, whereas the pretreatment with the proteasome inhibitor MG132 blocked both the curcumin-induced reduction of AP-2gamma and antiproliferative effect. Curcumin inhibited ErbB2 expression, and decreased the phosphorylation of Akt and ERK in NTera-2 cells. Conclusion: Curcumin induces apoptosis and inhibits proliferation in NTera-2 cells via the inhibition of AP-2gamma-mediated downstream cell survival signaling pathways.

[844]

TÍTULO / TITLE: - Systemic Therapy in Men with Metastatic Castration-resistant Prostate Cancer: A Systematic Review.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Loblaw DA; Walker-Dilks C; Winquist E; Hotte SJ
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RESUMEN / SUMMARY: - AIMS: Since 2004, docetaxel-based chemotherapy has been the standard of care for men with metastatic castration-resistant prostate cancer (mCRPC), but recently randomised controlled trials (RCTs) of novel agents have shown promise in extending overall survival. These trials have evaluated agents delivered before chemotherapy, to replace or supplement docetaxel, or addressed treatment options for men who have progressed on docetaxel therapy. This review was undertaken to determine which systemic therapies improve cancer- or patient-related outcomes in men with mCRPC.

MATERIALS AND METHODS: Searches were carried out in MEDLINE, EMBASE, the Cochrane Library and relevant conference proceedings. Eligible articles included RCTs comparing systemic therapy or combination (excluding primary or secondary androgen deprivation therapy, bone protective agents or radionuclides) with placebo or other agents in men with mCRPC. RESULTS: Twenty-five RCTs met the selection criteria. In chemotherapy-naive patients, targeted therapy with tasquinimod conferred a benefit in progression-free survival. Immunotherapy with sipuleucel-T extended overall survival and was well tolerated, but had no effect on the time to disease progression. Hypercastration with abiraterone extended progression-free survival, whereas overall survival was improved but not statistically proven. In the chemotherapy setting, updated and new trials of docetaxel alone confirmed the survival benefit seen in previous studies. A survival benefit with the addition of estramustine to docetaxel shown in a previous study did not lead to an improvement in pain palliation or quality of life. Trials of combining targeted therapies with docetaxel generally did not extend survival. The addition of bevacizumab improved progression-free survival, but not overall survival. The addition of GVAX immunotherapy or calcitriol was harmful. In the post-chemotherapy setting, progression-free and overall survival benefits were detected with cabazitaxel, abiraterone and enzalutamide. Cabazitaxel was associated with greater toxicity, whereas abiraterone and enzalutamide had less severe adverse effects. Satraplatin and sunitinib both extended progression-free survival, but did not improve overall survival. CONCLUSION: Docetaxel-based chemotherapy remains the standard of care in men with mCRPC who are candidates for palliative systemic therapy. Promising results are emerging with sipuleucel-T and abiraterone in the pre-docetaxel setting and cabazitaxel, abiraterone and enzalutamide in patients who progress on or after docetaxel. Further research to determine the optimal choice, sequence or even the combination of these agents is necessary.
TÍTULO / TITLE: Homeostatic housecleaning effect of selenium: Evidence that noncytotoxic oxidant-induced damage sensitizes prostate cancer cells to organic selenium-triggered apoptosis.

RESUMEN / SUMMARY: The anti-cancer activity of organic selenium has been most consistently documented at supra-nutritional levels at which selenium-dependent, antioxidant enzymes are maximized in both expression and activity. Thus, there is a strong imperative to identify mechanisms other than antioxidant protection to account for selenium’s anti-cancer activity. In vivo work in dogs showed that dietary selenium supplementation decreased DNA damage but increased apoptosis in the prostate, leading to a new hypothesis: Organic selenium exerts its cancer preventive effect by selectively increasing apoptosis in DNA-damaged cells. Here, we test whether organic selenium (methylseleninic acid; MSA) triggers more apoptosis in human and canine prostate cancer cells that have more DNA damage (strand breaks) created by hydrogen-peroxide (H2 O2) at noncytotoxic doses prior to MSA exposure. Apoptosis triggered by MSA was significantly higher in H2 O2-damaged cells. A supra-additive effect was observed—the extent of MSA-triggered apoptosis in H2 O2-damaged cells exceeded the sum of apoptosis induced by MSA or H2 O2 alone. However, neither the persistence of H2 O2-induced DNA damage, nor the activation of mitogen-activated protein kinases was required to sensitize cells to MSA-triggered apoptosis. Our results document that selenium can exert a “homeostatic housecleaning” effect— a preferential elimination of DNA-damaged cells. This work introduces a new and potentially important perspective on the anti-cancer action of selenium in the aging prostate that is independent of its role in antioxidant protection. © 2013 BioFactors, 2013.

[846]

TÍTULO / TITLE: Hydroxytyrosol Promotes Superoxide Production and Defects in Autophagy Leading to Anti-Proliferative and Apoptotic Effects on Human Prostate Cancer Cells.

RESUMEN / SUMMARY: The anti-cancer activity of organic selenium has been most consistently documented at supra-nutritional levels at which selenium-dependent, antioxidant enzymes are maximized in both expression and activity. Thus, there is a strong imperative to identify mechanisms other than antioxidant protection to account for selenium’s anti-cancer activity. In vivo work in dogs showed that dietary selenium supplementation decreased DNA damage but increased apoptosis in the prostate, leading to a new hypothesis: Organic selenium exerts its cancer preventive effect by selectively increasing apoptosis in DNA-damaged cells. Here, we test whether organic selenium (methylseleninic acid; MSA) triggers more apoptosis in human and canine prostate cancer cells that have more DNA damage (strand breaks) created by hydrogen-peroxide (H2 O2) at noncytotoxic doses prior to MSA exposure. Apoptosis triggered by MSA was significantly higher in H2 O2-damaged cells. A supra-additive effect was observed—the extent of MSA-triggered apoptosis in H2 O2-damaged cells exceeded the sum of apoptosis induced by MSA or H2 O2 alone. However, neither the persistence of H2 O2-induced DNA damage, nor the activation of mitogen-activated protein kinases was required to sensitize cells to MSA-triggered apoptosis. Our results document that selenium can exert a “homeostatic housecleaning” effect— a preferential elimination of DNA-damaged cells. This work introduces a new and potentially important perspective on the anti-cancer action of selenium in the aging prostate that is independent of its role in antioxidant protection. © 2013 BioFactors, 2013.

[846]
Hydroxytyrosol, an important polyphenolic compound found in olive oil, has shown anti-tumor activity both in vitro and in vivo. However, effects of hydroxytyrosol on prostate cancer are largely unknown. We found that hydroxytyrosol preferentially reduces the viability of human prostate cancer cells (PC-3, DU145) compared to an immortalized non-malignant prostate epithelial cell line (RWPE-1). Exposure of PC-3 cells to 80 micromol/L hydroxytyrosol resulted in significant increases in both superoxide production and activation of apoptosis. These increases were accompanied by mitochondrial dysfunction, defects in autophagy, and activation of MAP kinases. Moreover, N-acetyl-cysteine (NAC), an efficient reactive oxygen species (ROS) scavenger, was able to reverse the hydroxytyrosol-induced effects of cell viability loss, defects in autophagy, and activation of apoptosis. This evidence suggests that ROS play a vital role in the loss of PC-3 cell viability. However, MAPK inhibitors including U0126 (for Erk1/2), SB203580 (for p38MAPK) and SP600125 (for JNK) did not decrease hydroxytyrosol-induced growth inhibition, suggesting that these kinases may not be required for the growth inhibitory effect of hydroxytyrosol. Moreover, addition of ROS scavengers (i.e. NAC, catalase, pyruvate, SOD) in the growth media can prevent hydroxytyrosol induced cell viability loss, suggesting that extracellular ROS (superoxide and hydrogen peroxide) facilitate the anti-proliferation effect of hydroxytyrosol in prostate cancer cells. The present work firstly shows that hydroxytyrosol induces apoptotic cell death and mitochondrial dysfunction by generating superoxide in PC-3 cells. This research presents preliminary evidence on the in vitro chemopreventive effect of hydroxytyrosol, and will contribute to further investigation of hydroxytyrosol as an anti-cancer agent.
TÍTULO / TITLE: - Molecular lipidomics of exosomes released by PC-3 prostate cancer cells.

RESUMEN / SUMMARY: - The molecular lipid composition of exosomes is largely unknown. In this study, sophisticated shotgun and targeted molecular lipidomic assays were performed for in-depth analysis of the lipidomes of the metastatic prostate cancer cell line, PC-3, and their released exosomes. This study, based in the quantification of approximately 280 molecular lipid species, provides the most extensive lipid analysis of cells and exosomes to date. Interestingly, major differences were found in the lipid composition of exosomes compared to parent cells. Exosomes show a remarkable enrichment of distinct lipids, demonstrating an extraordinary discrimination of lipids sorted into these microvesicles. In particular, exosomes are highly enriched in glycosphingolipids, sphingomyelin, cholesterol, and phosphatidylserine (mol% of total lipids). Furthermore, lipid species, even of classes not enriched in exosomes, were selectively included in exosomes. Finally, it was found that there is an 8.4-fold enrichment of lipids per mg of protein in exosomes. The detailed lipid composition provided in this study may be useful to understand the mechanism of exosome formation, release and function. Several of the lipids enriched in exosomes could potentially be used as cancer biomarkers.


AUTORES / AUTHORS: - Llorente A; Skotland T; Sylvanne T; Kauhanen D; Rog T; Orlowski A; Vattulainen I; Ekroos K; Sandvig K

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RESUMEN / SUMMARY: - The molecular lipid composition of exosomes is largely unknown. In this study, sophisticated shotgun and targeted molecular lipidomic assays were performed for in-depth analysis of the lipidomes of the metastatic prostate cancer cell line, PC-3, and their released exosomes. This study, based in the quantification of approximately 280 molecular lipid species, provides the most extensive lipid analysis of cells and exosomes to date. Interestingly, major differences were found in the lipid composition of exosomes compared to parent cells. Exosomes show a remarkable enrichment of distinct lipids, demonstrating an extraordinary discrimination of lipids sorted into these microvesicles. In particular, exosomes are highly enriched in glycosphingolipids, sphingomyelin, cholesterol, and phosphatidylserine (mol% of total lipids). Furthermore, lipid species, even of classes not enriched in exosomes, were selectively included in exosomes. Finally, it was found that there is an 8.4-fold enrichment of lipids per mg of protein in exosomes. The detailed lipid composition provided in this study may be useful to understand the mechanism of exosome formation, release and function. Several of the lipids enriched in exosomes could potentially be used as cancer biomarkers.

TÍTULO / TITLE: - Diagnostic and Prognostic Role of Immunohistochemical Expression of Napsin-A Aspartic Peptidase in Clear Cell and Papillary Renal Cell Carcinoma: A Study Including 233 Primary and Metastatic Cases.

RESUMEN / SUMMARY: - The molecular lipid composition of exosomes is largely unknown. In this study, sophisticated shotgun and targeted molecular lipidomic assays were performed for in-depth analysis of the lipidomes of the metastatic prostate cancer cell line, PC-3, and their released exosomes. This study, based in the quantification of approximately 280 molecular lipid species, provides the most extensive lipid analysis of cells and exosomes to date. Interestingly, major differences were found in the lipid composition of exosomes compared to parent cells. Exosomes show a remarkable enrichment of distinct lipids, demonstrating an extraordinary discrimination of lipids sorted into these microvesicles. In particular, exosomes are highly enriched in glycosphingolipids, sphingomyelin, cholesterol, and phosphatidylserine (mol% of total lipids). Furthermore, lipid species, even of classes not enriched in exosomes, were selectively included in exosomes. Finally, it was found that there is an 8.4-fold enrichment of lipids per mg of protein in exosomes. The detailed lipid composition provided in this study may be useful to understand the mechanism of exosome formation, release and function. Several of the lipids enriched in exosomes could potentially be used as cancer biomarkers.


AUTORES / AUTHORS: - Xu B; Abourbih S; Sircar K; Kassouf W; Aprikian A; Tanguay S; Brimo F
**INSTITUCIÓN / INSTITUTION:** - Departments of *Pathology daggerUrology, McGill University Health Center, Montreal, QC, Canada double daggerDepartment of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX.

**RESUMEN / SUMMARY:** - Napsin-A aspartic peptidase (napsin-A) is an aspartic protease that is predominantly expressed in the proximal renal tubules and type II pneumocytes of the lung. Recently, napsin-A was reported to be present in a proportion of renal cell carcinomas (RCCs). However, the utilization of napsin-A immunohistochemistry as a routine diagnostic tool for RCC, and the correlation of the level of napsin-A expression with histologic features have not yet been established. In the current study, using tissue microarrays composed of primary and metastatic RCCs, napsin-A expression was demonstrated in 86 of 222 (39%) clear cell RCCs (CRCCs) and 16 of 21 (76%) papillary RCCs (PRCCs), with a strong and diffuse staining pattern observed in PRCCs and a relatively weak and focal positivity in CRCCs. Compared with primary CRCCs, a comparable proportion of metastatic CRCCs retained napsin-A expression (45/132, 34%), suggesting the potential utility of napsin-A in the evaluation of metastatic tumors. The expression of napsin-A was also found to be inversely correlated to aggressive local tumor characteristics, such as advanced pathologic stage and high Fuhrman nuclear grade. We conclude that napsin-A may be a valuable immunohistochemical marker in the diagnosis of RCCs, particularly PRCC.

[850]

**TÍTULO / TITLE:** - High-resolution transrectal ultrasound: Pilot study of a novel technique for imaging clinically localized prostate cancer

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


- Enlace al texto completo (gratuito o de pago)

1016/j.urolonc.2013.01.006

**AUTORES / AUTHORS:** - Pavlovich CP; Cornish TC; Mullins JK; Fradin J; Mettee LZ; Connor JT; Reese AC; Askin FB; Luck R; Epstein JI; Burke HB

**INSTITUCIÓN / INSTITUTION:** - James Buchanan Brady Urological Institute, Johns Hopkins Medical Institutions, Baltimore, MD. Electronic address: cpavlov2@jhmi.edu.

**RESUMEN / SUMMARY:** - OBJECTIVES: To determine how high-resolution transrectal ultrasound (HiTRUS) compares with conventional TRUS (LoTRUS) for the visualization of prostate cancer. METHODS AND MATERIALS: Twenty-five men with known prostate cancer scheduled for radical prostatectomy were preoperatively imaged with both LoTRUS (5MHz) and HiTRUS (21MHz). Dynamic cine loops and still images for each modality were saved and subjected to blinded review by a radiologist looking for hypoechoic foci/>=5mm.
in each sextant of the prostate. Following prostatectomy, areas of prostate cancer \( \geq 5 \) mm on pathologic review were anatomically correlated to LoTRUS and HiTRUS findings. The accuracy of LoTRUS and HiTRUS to visualize prostate cancer in each sextant of the prostate and to identify high-grade and locally advanced disease was assessed. The McNemar test was used to compare sensitivity and specificity and paired dichotomous outcomes between imaging modalities. RESULTS: Among 69 sextants with pathologically identified cancerous foci at radical prostatectomy, HiTRUS visualized 45 and missed 24, whereas LoTRUS visualized 26 and missed 43. Compared with LoTRUS, HiTRUS demonstrated improved sensitivity (65.2% vs. 37.7%) and specificity (71.6% vs. 65.4%). HiTRUS’s agreement with pathologic findings was twice as high as LoTRUS \( (P = 0.006) \). HiTRUS provided a nonsignificant increase in visualization of high-grade lesions \( (84\% \text{ vs. } 60\%, \ P = 0.11) \). CONCLUSIONS: HiTRUS appears promising for prostate cancer imaging. Our initial experience suggests superiority to LoTRUS for the visualization of cancerous foci, and supports proceeding with a clinical trial in the biopsy setting.

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[851]
**TÍTULO / TITLE:** - Radiation therapy for prostate cancer.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary]

**AUTORES / AUTHORS:** - Koontz BF; Lee WR

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**RESUMEN / SUMMARY:** - Radiation therapy is an effective treatment for newly diagnosed prostate cancer, salvage treatment, or for palliation of advanced disease. Herein we briefly discuss the indications, results, and complications associated with brachytherapy and external beam radiotherapy, when used as monotherapy and in combination with each other or androgen deprivation.

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[852]
**TÍTULO / TITLE:** - Editorial Comment to Radical cystectomy and orthotopic urinary diversion in male patients with pT4a urothelial bladder carcinoma: Oncological outcomes.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary]

**AUTORES / AUTHORS:** - Kitamura H

RESUMEN / SUMMARY: - First-line treatment based on androgen suppression is initially very effective in relieving the symptoms of metastatic prostate cancer. When androgen suppression no longer controls disease progression and symptoms, which treatments are known to improve duration or quality of survival? To answer this question, we reviewed the evidence using the standard Prescrire methodology. Low doses of corticosteroids, such as prednisone 5 to 10 mg per day, appear to improve quality of life for a few months by relieving symptoms in 20% to 40% of patients. When added to prednisone, docetaxel, a cytotoxic drug, tends to be more effective than mitoxantrone in terms of pain relief and quality of life. Docetaxel prolongs survival by about 2 months but provokes severe adverse effects in one-quarter of patients. Adding estramustine to this combination prolongs survival but carries a risk of serious thromboembolic events. Addition of bevacizumab has no proven impact on survival. After failure of cytotoxic chemotherapy with docetaxel, two hormonal treatments, abiraterone and enzalutamide, appear to prolong survival by about 4 or 5 months, and are associated with moderate adverse effects. However, these results are based on only one trial of each drug. Cabazitaxel is also moderately effective in terms of survival but has a less favourable adverse effect profile than abiraterone. A meta-analysis of trials of bisphosphonates used to prevent complications of bone metastases showed no major benefit, including in terms of pain relief. Bisphosphonates are not sufficiently effective to justify exposing patients to their potentially serious adverse effects. In one trial, the harm-benefit balance of denosumab was no better than that of zoledronic acid, a bisphosphonate. External beam radiation therapy or intravenous infusion of strontium-89 (a radioisotope) each relieves pain associated with bone metastases in over 70% of cases. If metastatic prostate cancer progresses despite androgen suppression, the two main options in 2012 are either: palliative treatment with corticosteroids and external beam radiation therapy or radioisotope infusion; or docetaxel followed by abiraterone, which slightly prolongs survival but at a cost of sometimes serious adverse effects.
TÍTULO / TITLE: - Treating octogenarians with muscle-invasive bladder cancer: Preoperative opportunities for increasing the benefits of surgical intervention.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Bassett JC; Chang SS

INSTITUCIÓN / INSTITUTION: - Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, TN. Electronic address: jeffrey.bassett@vanderbilt.edu.

RESUMEN / SUMMARY: - The question posed to the authors is whether surgery is the best treatment option for octogenarians with invasive bladder cancer. Herein, we detail the rationale in favor of radical cystectomy and opportunities for improvement in the processes of care for those who may be surgical candidates.

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TÍTULO / TITLE: - Inhibition of presenilins attenuates proliferation and invasion in bladder cancer cells through multiple pathways.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Gai JW; Wahafu W; Hsieh YC; Liu M; Zhang L; Li SW; Zhang B; He Q; Guo H; Jin J

INSTITUCIÓN / INSTITUTION: - Department of Urology, Peking University First Hospital; Institute of Urology, Peking University, Beijing, China.

RESUMEN / SUMMARY: - OBJECTIVE: Presenilin (PS)/gamma-secretase is a key protease that initiates various biological processes. We investigated the effect of PS/gamma-secretase on the expression and inhibition of urothelial cell carcinoma of bladder (UCB) as a potential alternative therapeutic target for UCB. MATERIALS AND METHODS: PS-1 and PS-2 were identified in normal and malignant human bladder transitional cells by immunohistochemistry. We blocked PSs using a PS/gamma-secretase inhibitor N-(N-[3,5-difluorophenacetyl]-L-alanyl)-S-phenylglycine-t-butylerster (DAPT), and the proliferative and invasive potential of UCB cells SW780, BIU-87, 5637, and T24, and human normal urothelial cell line SV-HUC-1 were analyzed using Western blot, cell viability test, flow cytometry, and transwell assay. All experiments were repeated at least 3 times. RESULTS: Human bladder samples of UCB, SW780,
BIU-87, 5637, and T24 cells expressed higher PS-1 compared with normal ones. Cell vitality test demonstrated that DAPT attenuated UCB cell proliferation more than SV-HUC-1. Flow cytometry and transwell assay showed that T24 cells were arrested at G1/S checkpoint and its invasive ability was impaired. Western blot assay markedly showed that protein levels of CD44-intracellular domain, insulinlike growth factor-1Rbeta, extracellular regulated protein kinase ½, cyclin D1, proliferating cell nuclear antigen, and matrix metalloproteinase-9 were downregulated by DAPT, whereas vascular endothelial growth factor receptor-2 and vascular endothelial growth factor-165 were upregulated. CONCLUSIONS: Our study revealed that PS-1 might be implicated in the proliferation and invasion of UCB, and that it may serve as a potential therapeutic target for UCB, but further studies are warranted to verify the effects of inhibition of PS/gamma-secretase on angiogenesis.

[856]

TÍTULO / TITLE: - Sunitinib induces cellular senescence via p53/Dec1 activation in renal cell carcinoma cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1111/cas.12176
AUTORES / AUTHORS: - Zhu Y; Xu L; Zhang J; Hu X; Liu Y; Yin H; Lv T; Zhang H; Liu L; An H; Liu H; Xu J; Lin Z
INSTITUCIÓN / INSTITUTION: - Department of Urology, Ninth People’s Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China; Department of Urology, Zhongshan Hospital, Fudan University, Shanghai, China.

RESUMEN / SUMMARY: - Although multtargeted tyrosine kinase inhibitor sunitinib has been used as first-line therapeutic agent against metastatic renal cell carcinoma (mRCC), the molecular mechanism and functional role per se for its therapeutic performance remains obscure. Our present study revealed that sunitinib-treated RCC cells exhibit senescence characteristics including increased SA-beta-gal activity, DcR2 and Dec1 expression, and senescence-associated secretary phenotype (SASP) such as proinflammatory cytokines interleukin (IL)-1alpha, IL-6 and IL-8 secretion. Moreover, sunitinib administration also led to cell growth inhibition, G1-S cell cycle arrest and DNA damage response in RCC cells, suggesting therapeutic significance of sunitinib-induced RCC cellular senescence. Mechanistic investigations indicated that therapy-induced senescence (TIS) following sunitinib treatment mainly attributed to p53/Dec1 signaling activation mediated by Raf-1/NF-kappaB inhibition in vitro. Importantly, in vivo study showed tumor growth inhibition and prolonged overall survival were associated with increased p53 and Dec1 expression, decreased Raf-1 and Ki67 staining, and upregulated SA-beta-gal
activity after sunitinib treatment. Immunohistochemistry analysis of tumor tissues from RCC patients receiving sunitinib neoadjuvant therapy confirmed the similar treating phenotype. Taken together, our findings suggested that sunitinib treatment performance could be attributable to TIS, depending on p53/Dec1 activation via inhibited Raf-1/nuclear factor (NF)-kappaB activity. These data indicated potential insights into therapeutic improvement with reinforcing TIS-related performance or overcoming SASP-induced resistance.

[857]
**TÍTULO / TITLE:** - Association between the high risk occupations and bladder cancer in Iran: A case-control study.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**AUTORES / AUTHORS:** - Khoubi J; Pourabdian S; Mohebbi I; Tajvidi M; Zaroorian O; Giahi O
**INSTITUCIÓN / INSTITUTION:** - Department of Occupational Health, Faculty of Health, Kurdistan University of Medical Sciences, Kurdistan, Iran.
**RESUMEN / SUMMARY:** - OBJECTIVES: The objective of this work was to identify the high-risk occupations in Iran and to re-inspect occupations that were related to bladder cancer. MATERIALS AND METHODS: In the study, 300 patients suffering from bladder cancer and 500 control individuals were interviewed. Demographic information, occupational history, and history of exposure to chemical compounds such as aromatic amines for each participant were collected. ORs and 95% CIs were calculated using unconditional logistic regression for each occupation. RESULTS: There was a significantly increased risk of bladder cancer among truck and bus drivers (OR = 11.3), skilled agricultural, forestry and fishery workers (OR = 6.0), metal industry workers (OR = 6.0), domestic housekeepers (OR = 5.9), and construction workers (OR = 3.8). CONCLUSIONS: The study showed a strong correlation between truck and bus drivers, skilled agricultural, forestry and fishery workers, metal industry workers, domestic housekeepers, as well as construction workers and the increased risk of bladder cancer in these occupations.

[858]
**TÍTULO / TITLE:** - A population-based study comparing HRQoL among breast, prostate, and colorectal cancer survivors to propensity score matched controls, by cancer type, and gender.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
BACKGROUND: Objectives were to compare health-related quality of life (HRQoL) between breast cancer survivors, prostate cancer survivors (PCS), and colorectal cancer survivors (CCS) to matched controls, stratified by short and long-term survivors, by cancer type, and gender.

METHODS: By using the 2009 Behavioral Risk Factor Surveillance System, propensity scores matched three controls to adult survivors >1 year past diagnosis (N = 11,964) on age, gender, race/ethnicity, income, insurance status, and region of the USA. Chi-square tests and logistic regression models compared HRQoL outcomes (life satisfaction, activity limitations, sleep quality, emotional support, general, physical, and mental health). RESULTS: Although all cancer survivors reported worse general health (p < 0.000) and more activity limitations (p < 0.004) than controls, these disparities decreased among long-term survivors. Short-term PCS and male CCS were more likely to report worse outcomes across additional domains of HRQoL than controls, but PCS were 0.61, 0.63, and 0.70 times less likely to report activity limitations, fair/poor general health, and 1-15 bad physical health days in the past month than male CCS. Breast cancer survivors and female CCS were 2.12 and 3.17, 1.58 and 1.86, and 1.49 and 153, respectively, times more likely to report rarely/never receiving needed emotional support, 1-15 bad mental health days in the past month, and not receiving enough sleep 1-15 days in the past month than PCS and male CCS. CONCLUSIONS: Cancer survivors experience worse HRQoL than similar individuals without a history of cancer and the severity of affected HRQoL domains differ by time since diagnosis, cancer type, and gender.

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RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


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RESUMEN / SUMMARY: - The synthesis of 7alpha-testosterone-chlorambucil hybrid is reported. This compound is made from testosterone in a 6 step reaction sequence and with 23% overall yield. An alternative convergent reaction sequence yielded the same hybrid through a Grubbs metathesis reaction between chlorambucil allyl ester and 7alpha-allyltestosterone with 35% overall yield. MTT assays showed that the hybrid is selective towards hormone-dependent prostate cancer cell line (LNCaP (AR+)) and shows similar activity than the parent drug, chlorambucil. Thus, the new hybrid shows promising potential for drug targeting of hormone-dependent prostate cancer through its capacity of delivering chlorambucil directly to the site of treatment. This could extend the use of chlorambucil to prostate cancer in the future.

[860]
TÍTULO / TITLE: - Current treatments for renal failure due to multiple myeloma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   Enlace al texto completo (gratuito o de pago)
1517/14656566.2013.803068
AUTORES / AUTHORS: - Kastritis E; Terpos E; Dimopoulos MA
INSTITUCIÓN / INSTITUTION: - University of Athens, School of Medicine, Department of Clinical Therapeutics, Athens, Greece.
RESUMEN / SUMMARY: - Introduction: Renal impairment (RI) is a common complication of symptomatic myeloma; 20 - 40% of newly diagnosed patients present with moderate or severe RI and 10% of them may require dialysis. Immediate initiation of specific antimyeloma therapy is crucial in order to improve RI. Areas covered: There has been a significant improvement in the outcome of patients with RI over the past 15 years. The authors review current data on the role of antimyeloma therapy on the improvement or resolution of RI and the importance of novel regimens, especially those based on bortezomib. IMiDs-based regimens, conventional chemotherapy and high-dose therapy is also reviewed. The role of extrarenal free light chain removal, by means of plasma exchange or extended hemodialysis with the use of high cutoff dialysis membranes, is also discussed. Expert opinion: Bortezomib/dexamethasone-based regimens are the preferred regimens for most patients with multiple myeloma (MM) who present with RI, especially for newly diagnosed patients; however, other novel agents (thalidomide, lenalidomide) in combination with dexamethasone may also improve RI in several patients. Further investigation is needed for the clarification of the role of plasma exchange or extended high cutoff dialysis. Carfilzomib, which was recently approved, may also be a treatment choice for selected patients with relapsed MM and RI.
**TÍTULO / TITLE:** - Expression of Secreted Frizzled-Related Protein 1 and 3, T-cell Factor 1 and Lymphoid Enhancer Factor 1 in Clear Cell Renal Cell Carcinoma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Pathol Oncol Res. 2013 Apr 10.

**AUTORES / AUTHORS:** - Nikuseva-Martic T; Serman L; Zeljko M; Vidas Z; Gasparov S; Zeljko HM; Kosovic M; Pecina-Slaus N

**INSTITUCIÓN / INSTITUTION:** - Department of Biology, School of Medicine, University of Zagreb, Salata 3, 10000, Zagreb, Croatia, tmartic@mef.hr.

**RESUMEN / SUMMARY:** - Frequency and mortality of renal cell carcinoma (RCC) are increasing for decades. However, the molecular background of RCC tumorigenesis is still poorly understood. In current study we investigated the expression of TCF/LEF and SFRP family members (SFRP1 and SFRP3) to gain a better understanding of biological signaling pathways responsible for epidemiology and clinical parameters of clear cell RCC (cRCC). Thirty-six pairs of paraffin-embedded clear cRCC and adjacent nontumoral tissues samples using immunohistochemistry (IHC) were analyzed and compared with corresponding clinicopathological parameters. Immunohistochemistry indicated statistically significant decreased SFRP3 expression in tumor tissues but no consistency in SFRP1 expression in analyzed normal and tumor tissue. The TCF1 expression level was significantly weaker in normal tissue compared to tumor samples while LEF1 protein levels were significantly weaker in tumor tissue. To our knowledge, this is the first report on analysis of the expression of transcription factors TCF1 and LEF1 in clear cell renal cell carcinoma and their comparison with Wnt signal pathway antagonists belonging to SFRP family.

**RESUMEN / SUMMARY:** - Focal ablation of prostate cancer: four roles for magnetic resonance imaging guidance.

**AUTORES / AUTHORS:** - Sommer G; Bouley D; Gill H; Daniel B; Pauly KB; Diederich C

**INSTITUCIÓN / INSTITUTION:** - Department of Radiology, Stanford University School of Medicine, Stanford, California 94305, USA.

**RESUMEN / SUMMARY:** - INTRODUCTION: There is currently a great deal of interest in the possible use of focal therapies for prostate cancer, since such treatments offer the prospect for control or cure of the primary disease with minimal side effects. Many forms of thermal therapy have been proposed for focal ablation of prostate cancer, including laser, high intensity ultrasound and
cryotherapy. This review will demonstrate the important roles that magnetic resonance imaging (MRI) guidance can offer to such focal ablation, focusing on the use of high intensity ultrasonic applicators as an example of one promising technique. MATERIALS AND METHODS: Transurethral and interstitial high intensity ultrasonic applicators, designed specifically for ablation of prostate tissue were tested extensively in vivo in a canine model. The roles of MRI in positioning the devices, monitoring prostate ablation, and depicting ablated tissue were assessed using appropriate MRI sequences. RESULTS: MRI guidance provides a very effective tool for the positioning of ablative devices in the prostate, and thermal monitoring successfully predicted ablation of prostate tissue when a threshold of 52 masculineC was achieved. Contrast enhanced MRI accurately depicted the distribution of ablated prostate tissue, which is resorbed at 30 days. CONCLUSIONS: Guidance of thermal therapies for focal ablation of prostate cancer will likely prove critically dependent on MRI functioning in four separate roles. Our studies indicate that in three roles: device positioning; thermal monitoring of prostate ablation; and depiction of ablated prostate tissue, MR techniques are highly accurate and likely to be of great benefit in focal prostate cancer ablation. A fourth critical role, identification of cancer within the gland for targeting of thermal therapy, is more problematic at present, but will likely become practical with further technological advances.
function strategy, we showed that transfection of PC-3M-MM2 cells with anti-
<i>miR-21</i>- and p47<i>phox</i>-siRNA (si-p47<i>phox</i>) led to reduced expression of <i>miR-21</i>
with concurrent increase in maspin and PDCD4, and decreased the invasiveness of the cells. Tail-vein injections of anti-
<i>miR-21</i>- and si-p47<i>phox</i>-transfected PC-3M-MM2 cells in severe combined immunodeficient (SCID) mice produce control sequences.
Clinical samples from patients with advanced prostate cancer expressed high levels of <i>miR-21</i> and <i>p47</i>, and low expression of maspin and PDCD4. Finally, ROS activates Akt in these cells, inhibition of which reduces <i>miR-21</i> expression. Innovation: The levels of NADPH oxidase-derived ROS are high in prostate cancer cells, which have been shown to be involved in their growth and migration. This study demonstrates that ROS produced by this pathway is essential for the expression and function of an onco-miR, <i>miR-21</i>, in androgen receptor negative prostate cancer cells. Conclusion: These data demonstrate that <i>miR-21</i> is an important target of ROS, which contributes to the highly invasive and metastatic phenotype of prostate cancer cells.

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This study demonstrates that ROS produced by this pathway is essential for the expression and function of an onco-miR, <i>miR-21</i>, in androgen receptor negative prostate cancer cells. Conclusion: These data demonstrate that <i>miR-21</i> is an important target of ROS, which contributes to the highly invasive and metastatic phenotype of prostate cancer cells.
was also assessed. RESULTS: Pharmacokinetic studies showed rapid clearance of 223Ra from the vasculature, with a median of 14% (range 9-34%), 2% (range 1.6-3.9%), and 0.5% (range 0.4-1.0%) remaining in plasma at the end of infusion, after 4 h, and after 24 h, respectively. Biodistribution studies showed early passage into the small bowel and subsequent fecal excretion with a median of 52% of administered 223Ra in the bowel at 24 h. Urinary excretion was relatively minor (median of 4% of administered 223Ra). Bone retention was prolonged. No dose-limiting toxicity was observed. Pharmacodynamic effects were observed (alkaline phosphatase and serum N-telopeptides) in a significant fraction of patients. CONCLUSION: 223Ra cleared rapidly from plasma and rapidly transited into small bowel, with fecal excretion the major route of elimination. Administered activities up to 200 kBq/kg were associated with few side effects and appeared to induce a decline in serum indicators of bone turnover.

[865]
{TITULO / TITLE}: - Perspectives on treatment of metastatic castration-resistant prostate cancer.
{RESUMEN / SUMMARY}: - Enlace al Resumen / Link to its Summary
{AUTORES / AUTHORS}: - Merseburger AS; Bellmunt J; Jenkins C; Parker C; Fitzpatrick JM
{INSTITUCIÓN / INSTITUTION}: - Department of Urology and Urologic Oncology, Hannover Medical School, Hannover, Germany;
{RESUMEN / SUMMARY}: - The arrival of several new agents-cabazitaxel, abiraterone acetate, enzalutamide, and radium-223-is changing the treatment options and management of patients with metastatic castration-resistant prostate cancer (mCRPC). Many other novel agents are also being investigated. As new drugs become approved, new treatment strategies and markers to best select which patients will best respond to which drug are needed. This review article is a summary of a European Treatment Practices Meeting, which was convened to discuss these latest data on novel agents and current treatment strategies in the mCRPC setting.

[866]
{TITULO / TITLE}: - Management of castrate resistant prostate cancer-recent advances and optimal sequence of treatments.
{RESUMEN / SUMMARY}: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Zhang TY; Agarwal N; Sonpavde G; Dilorenzo G; Bellmunt J; Vogelzang NJ

INSTITUCIÓN / INSTITUTION: - University of Utah, Huntsman Cancer Institute, 2000 Circle of Hope, Ste 2123, Salt Lake City, UT, 84112, USA.

RESUMEN / SUMMARY: - Until 2010, chemotherapy with docetaxel was the only approved agent for treatment of metastatic castrate resistant prostate cancer (mCRPC). Since then, the therapeutic landscape of mCRPC has changed rapidly. Multiple novel agents have received regulatory approval after demonstrating improved overall survival in separate randomized Phase 3 studies. These include immuno-therapeutic agent sipuleucel-T, androgen axis inhibitors abiraterone and enzalutamide, and a novel microtubule inhibitor cabazitaxel. More recently, radium-223, a bone-targeting alpha emitting radiopharmaceutical, was reported to improve skeletal related events, as well as overall survival in a Phase 3 randomized study. Additionally, there are several promising agents in the advanced stages of clinical development. Here, we describe the agents recently shown to improve overall survival, and those that have reached the advanced stages of development in Phase 3 clinical trials. We will also propose a strategy for optimal sequencing of these agents in the treatment of mCRPC.


TÍTULO / TITLE: - Interferon alfa in the treatment paradigm for non-muscle-invasive bladder cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Lamm D; Brausi M; O'Donnell MA; Witjes JA

INSTITUCIÓN / INSTITUTION: - BCG Oncology, P.C., Phoenix, AZ. Electronic address: dlamm@bcgoncology.com.

RESUMEN / SUMMARY: - OBJECTIVES: In this article, we review the various options for and the potential role of interferon alfa (IFN-alpha) in the treatment of non-muscle-invasive bladder cancer (NMIBC). METHODS: PubMed was searched for journal articles on IFN-alpha use in treating bladder cancer. The references listed in the National Comprehensive Cancer Network guidelines were used as a guide to identify relevant publications on treatments for NMIBC. RESULTS: Transurethral resection with adjuvant intravesical chemotherapy or
immunotherapy is the standard treatment option for NMIBC. Adjuvant IFN-alpha therapy has limited efficacy in preventing recurrences in intermediate-risk and high-risk patients; bacillus Calmette-Guerin (BCG) monotherapy is the recommended first-line treatment in these patients. Unfortunately, cancer progression or recurrence is a common outcome; radical cystectomy, which is often the lifesaving approach in such a scenario, is associated with significant morbidity, mortality, and decreased quality of life. Current alternatives to cystectomy include repeat intravesical immunotherapy, conventional instillation chemotherapy, and device-assisted intravesical chemotherapy. The efficacy of any chemotherapy after BCG failure, either conventional or device assisted, has not been established. BCG and IFN-alpha combination intravesical therapy has not been investigated thoroughly; based on available data, combination therapy appears to be most effective in patients with carcinoma in situ and may be preferentially considered as an alternative to radical cystectomy for patients with intermediate-risk or high-risk NMIBC who do not tolerate the standard BCG dose or experience BCG failure after 1 year of therapy. However, this approach requires close follow-up and should only be chosen after careful consideration of all risk factors. CONCLUSIONS: There is a lack of efficacious treatment options for patients with NMIBC recurrence or progression after initial BCG treatment. There is a need for well-designed clinical trials investigating the safety and efficacy of available therapies, including BCG and IFN-alpha2b combination therapy.

[868]

TÍTULO / TITLE: - Toll-like receptors in prostate infection and cancer between bench and bedside.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Gambara G; De Cesaris P; De Nunzio C; Ziparo E; Tubaro A; Filippini A; Riccioli A
INSTITUCIÓN / INSTITUTION: - Istituto Pasteur-Fondazione Cenci Bolognetti, Department of Anatomy, Histology, Forensic Medicine and Orthopaedics, Section of Histology and Medical Embryology, Sapienza University of Rome, Rome, Italy.
RESUMEN / SUMMARY: - Toll-Like receptors (TLRs) are a family of evolutionary conserved transmembrane proteins that recognize highly conserved molecules in pathogens. TLR-expressing cells represent the first line of defence sensing pathogen invasion, triggering innate immune responses and subsequently priming antigen-specific adaptive immunity. In vitro and in vivo studies on experimental cancer models have shown both anti- and pro-tumoural activity of different TLRs in prostate cancer, indicating these receptors as potential targets.
for cancer therapy. In this review, we highlight the intriguing duplicity of TLR stimulation by pathogens: their protective role in cases of acute infections, and conversely their negative role in favouring hyperplasia and/or cancer onset, in cases of chronic infections. This review focuses on the role of TLRs in the pathophysiology of prostate infection and cancer by exploring the biological bases of the strict relation between TLRs and prostate cancer. In particular, we highlight the debated question of how reliable mutations or deregulated expression of TLRs are as novel diagnostic or prognostic tools for prostate cancer. So far, the anticancer activity of numerous TLR ligands has been evaluated in clinical trials only in organs other than the prostate. Here we review recent clinical trials based on the most promising TLR agonists in oncology, envisaging a potential application also in prostate cancer therapy.

[869]
TÍTULO / TITLE: - Intermittent versus continuous androgen deprivation therapy in advanced prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Klotz L
INSTITUCIÓN / INSTITUTION: - Sunnybrook Health Sciences Centre, Division of Urology, University of Toronto, 2075 Bayview Ave. #MG408, Toronto, Ontario, M4N 3M5, Canada, laurence.klotz@sunnybrook.ca.
RESUMEN / SUMMARY: - Intermittent androgen deprivation is increasingly employed as an alternative to continuous life long androgen deprivation therapy for men with advanced or recurrent prostate cancer. Two recent phase III trials have clarified the benefits of intermittent therapy. In men with non-metastatic disease with PSA recurrence after definitive local therapy, intermittent therapy showed equivalent survival to continuous therapy, with significant improvements in quality of life. Patients on intermittent therapy experience improved bone health, less metabolic and hematologic disturbances, fewer hot flashes, as well as improved sexual function. In men with metastatic disease, the data is less clear. The long-awaited results of SWOG 9324 comparing intermittent to continuous therapy in metastatic disease showed a trend to worse outcome in the patients with ‘minimal’ metastatic disease, and no difference in those with widespread bone mets. The significance of this observation is in dispute. This review also addresses practical issues in the use intermittent therapy, including patient selection, follow-up and cycling of therapy. The recent results of randomized clinical trials now establish that intermittent androgen deprivation
therapy is an approach that should be considered the standard of care for most patients with non-metastatic prostate cancer requiring hormonal therapy.

[870]

**Título / Title:** Optimal therapy sequencing in metastatic castration-resistant prostate cancer.

**Resumen / Summary:** Prostate cancer is the most common cancer in men worldwide, accounting for approximately 242,000 new cases and 28,000 deaths annually in the USA. Although localized disease is often curable, advanced disease is generally not, especially when the cancer becomes castration-resistant and metastasizes to bone. Fortunately, advances in research have led to the recent approval of several novel therapies for the treatment of metastatic disease, and many other promising agents are in development. With this success arises the distinct challenge of optimizing both sequencing and the design of rational combinations with these agents. This review focuses on practical and experimental approaches to this challenge.


**Autores / Authors:** Abouharb S; Corn PG

**Institución / Institution:** Department of Genitourinary Medical Oncology, Unit 1374, MD Anderson Cancer Center, 1155 Pressler St., Houston, TX, 77030, USA.

**Resumen / Summary:** Prostate cancer is the most common cancer in men worldwide, accounting for approximately 242,000 new cases and 28,000 deaths annually in the USA. Although localized disease is often curable, advanced disease is generally not, especially when the cancer becomes castration-resistant and metastasizes to bone. Fortunately, advances in research have led to the recent approval of several novel therapies for the treatment of metastatic disease, and many other promising agents are in development. With this success arises the distinct challenge of optimizing both sequencing and the design of rational combinations with these agents. This review focuses on practical and experimental approaches to this challenge.

[871]

**Título / Title:** Functional role of microRNAs in prostate cancer and therapeutic opportunities.

**Resumen / Summary:** Prostate cancer is one of the most common causes of cancer-related death. The management of prostate cancer patients has become increasingly complex, consequently calling on the need for identifying and validating prognostic and predictive biomarkers. Growing evidence indicates that microRNAs play a crucial role in the pathobiology of neoplastic diseases. The deregulation of the cellular "miRNome" in prostate cancer has been connected with multiple tumor-promoting activities such as aberrant activation
of growth signals, anti-apoptotic effects, prometastatic mechanisms, alteration of the androgen receptor pathway, and regulation of the cancer stem cell phenotype. With the elucidation of molecular mechanisms controlled by microRNAs, investigations have been conducted in an attempt to exploit these molecules in the clinical setting. Moreover, the multifaceted biological activity of microRNAs makes them an attractive candidate as anticancer agents. This review summarizes the current knowledge on microRNA deregulation in prostate cancer, and the rationale underlying their exploitation as cancer biomarkers and therapeutics.

[872]
TÍTULO / TITLE: - Influence of androgen deprivation therapy on choline PET/CT in recurrent prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Dost RJ; Glaudemans AW; Breeuwsma AJ; de Jong IJ
INSTITUCIÓN / INSTITUTION: - Department of Urology, University of Groningen, University Medical Center Groningen, Hanzeplein 1, 9713 GZ, Groningen, The Netherlands, rj.dost@umcg.nl.
RESUMEN / SUMMARY: - PURPOSE: Recurrent prostate cancer is usually treated by combining radiotherapy and androgen deprivation therapy. To stage the cancer, choline positron emission tomography (PET)/CT can be performed. It is generally thought that androgen deprivation therapy does not influence choline PET/CT. In this article we focus on the molecular backgrounds of choline and androgens, and the results of preclinical and clinical studies performed using PET/CT. METHODS: Using PubMed, we looked for the relevant articles about androgen deprivation therapy and choline PET/CT. RESULTS: During ADT, a tendency of decreased uptake of choline in prostate cancer was observed, in particular in hormone-naive patients. CONCLUSION: We conclude that in order to prevent false-negative choline PET/CT scans androgen deprivation should be withheld prior to scanning, especially in hormone-naive patients.

[873]
TÍTULO / TITLE: - The Future of Systemic Therapies for Localised Prostate Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Dost RJ; Glaudemans AW; Breeuwsma AJ; de Jong IJ
In the last decade, many systemic therapies have become available to improve survival in the setting of castration-resistant prostate cancer. Once effective treatments for advanced and incurable disease have been established, these agents are generally explored in the adjuvant and neoadjuvant settings to evaluate their role in increasing the chance of cure for localised disease. Clinical trials evaluating new therapies in high-risk prostate cancer can broadly be divided into two categories. Phase III (and some phase II) trials generally evaluate treatments that have already been shown to provide clinical benefit in the advanced disease setting; whereas smaller phase I (and some phase II) trials often serve as proof-of-principle assessments in the development of novel agents. The goal of this review is to provide an overview of present and ongoing clinical trials of both of these categories, evaluating the promise of systemic therapies in the setting of high-risk localised prostate cancer. We undertook a search of Ovid Medline, Embase and clinicaltrials.gov for prospective clinical studies assessing systemic therapy for early stage prostate cancer, either before or after definitive local treatment (surgery or radiation) from 2000 onwards. This resulted in 53 studies, of which 29 were deemed worthy of this overview and are presented herein, broadly divided by mechanism of action. Clearly, the arena evaluating the future of systemic therapies for localised prostate cancer will be a very active one.

Association of the Charlson comorbidity index and hypertension with survival in men with metastatic castration-resistant prostate cancer?

OBJECTIVES: The independent prognostic effect of comorbidities on outcomes in men with metastatic castration-resistant prostate cancer (mCRPC) is unclear. We sought to determine whether the Charlson comorbidity index (CCI) and hypertension (HTN) are associated with overall survival (OS) independent of known clinical prognostic factors in mCRPC.
PATIENTS AND METHODS: A retrospective analysis was conducted on 221 patients with mCRPC treated with docetaxel plus prednisone combined with AT-101 (bcl-2 antagonist) or placebo on a prospective randomized phase II trial. The Cox regression analysis was performed to identify whether the CCI or HTN or both (by medical history) independently predicted OS after adjusting for baseline variables known to be associated with OS. The Wilcoxon rank sum test and the Fisher exact test were used to compare data by comorbidity groups (CCI as a continuous variable, CCI = 6 vs. CCI >/= 7 and HTN vs. no HTN).

RESULTS: The CCI was 6 in 116 patients (52.7%), 7 in 70 (31.8%), 8 in 23 (10.5%), 9 in 4 (1.8%), and 10 in 7 patients (3.2%). HTN was present in 107 (48.6%) patients. Patients with CCI of >/=7 were older and exhibited worse performance status and anemia than patients with CCI of 6 (P<0.05). The CCI was not independently predictive of OS on univariable and multivariable analyses. HTN alone or in combination with the CCI was borderline significantly associated with OS (P ~0.09) on both univariable and multivariable analyses.

CONCLUSIONS: The CCI did not predict OS independent of known prognostic factors in mCRPC. Age, performance status, and anemia may adequately capture comorbidities in the context of mCRPC, given their association with higher CCI. Further prospective study of comorbidities in a larger data set may be warranted. The study of HTN in a larger data set may also be warranted given its borderline-independent association with OS.

[875]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Botta F; Cremonesi M; Ferrari ME; Amato E; Guerriero F; Vavassori A; Sarnelli A; Severi S; Pedrol G; Paganelli G

INSTITUCIÓN / INSTITUTION: - Medical Physics Unit, European Institute of Oncology, Milan, Italy.

RESUMEN / SUMMARY: - PURPOSE: A novel method for prostate irradiation is investigated. Similarly to 125I or 103Pd seed brachytherapy, 90Y-avidin could be injected via the perineum under ultrasound image guidance. This study inspects the theoretical feasibility with a dosimetric model based on Monte Carlo simulation. METHODS: A geometrical model of the prostate, urethra and rectum was designed. The linear-quadratic model was applied to convert 125I absorbed dose prescription/constraints into 90Y dose through biological effective dose (BED) calculation. The optimal 90Y-avidin injection strategy for the present model was obtained. Dose distribution was calculated by Monte Carlo simulation.
Carlo simulation (PENELOPE, GEANT4). Dose volume histograms (DVH) for the prostate, urethra and rectum were compared to typical DVHs of 125I seed brachytherapy, used routinely in our institute. RESULTS: With 90Y-avidin, at least 95% of the prostate must receive more than 70 Gy. The absorbed dose to 10% of the urethra (D10%_urethra) and the maximum absorbed dose to the rectum (Dmax_rectum) must be lower than 122 Gy. For the present model, the optimum strategy consists in multiple injections of 90Y-avidin 50 μl drops, for a total volume of 3.1 ml. The minimum activity to deliver the prescribed absorbed dose is 0.7 GBq, which also fully respects urethral and rectal constraints. The resulting dose map has a maximum in the central region with a sharp decrease towards the urethra and the prostate edge. Notably, D10%_urethra is 95 Gy and Dmax_rectum is below 2 Gy. Prostate absorbed dose is higher with 90Y-avidin than 125I seeds, although the total volume receiving the prescribed absorbed dose is 1-2% lower. Urethral DVH strictly depends on the 90Y distribution, to be optimized according to prostate shape; in our model, BED30%_urethra is 90 Gy with 90Y-avidin, whereas for patients receiving 125I seeds it ranges between 150 and 230 Gy. The rectal DVH is always more favourable with 90Y. CONCLUSION: The methodology is theoretically feasible and can deliver an effective treatment in T1-T2 prostate cancer. Pharmacokinetic and biodistribution studies in prostate cancer patients are needed for validation.
Multivariate analysis revealed that unmarried men had a 40% increase in the relative risk of prostate cancer-specific mortality (HR 1.40; CI 1.35-1.44; p < 0.0001), and a 51% increase in overall mortality (HR 1.51; CI 1.48-1.54; p < 0.0001), even when controlling for age, AJCC stage, tumor grade, race and median household income. Furthermore, the 5 year disease-specific survival rates for married men was 89.1% compared to 80.5% for unmarried men (p < 0.0001). CONCLUSION: Marital status is an independent predictor of prostate cancer-specific mortality and overall mortality in men with prostate cancer. Unmarried men have a higher risk of prostate cancer-specific mortality compared to married men of similar age, race, stage, and tumor grade.

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TÍTULO / TITLE: linc-UBC1 physically associates with polycomb repressive complex 2 (PRC2) and acts as a negative prognostic factor for lymph node metastasis and survival in bladder cancer.

RESUMEN / SUMMARY: OBJECTIVES: The human genome encodes many long intergenic noncoding RNAs (lincRNAs). However, their biological functions, molecular mechanisms and prognostic values associated with bladder cancer remain to be elucidated. Here we investigated a lincRNA termed linc-UBC1 (Up-regulated in bladder cancer 1) and evaluated its prognostic value in bladder cancer patients. MATERIALS AND METHODS: Expression of linc-UBC1 was evaluated by quantitative reverse transcription PCR (qRT-PCR) in 102 bladder cancer tissue samples and normal adjacent tissues. The functions of linc-UBC1 on cell proliferation, migration, invasion, colony formation, tumorigenicity and metastatic potential were evaluated by knockdown strategy in vitro and in vivo. RNA immunoprecipitation (RIP) was performed to confirm that linc-UBC1 physically associates with EZH2 and SUZ12, core components of polycomb repressive complex 2 (PRC2). Chromatin immunoprecipitation (ChIP) was conducted to examine histone modification status. RESULTS: qRT-PCR confirmed that linc-UBC1 expression is up-regulated in 60 cases (58.8%) in bladder cancer tissues compared with normal adjacent tissues, and its overexpression correlates with lymph node metastasis and poor survival.
Further functional analysis demonstrated that knockdown of linc-UBC1 attenuates bladder cancer cell proliferation, motility, invasion, colony formation ability, tumorigenicity and metastatic potential. Importantly, the inhibitory effect of linc-UBC1 on cell proliferation was also observed in primary bladder cancer cells obtained from patients. RIP and ChIP assay confirmed that linc-UBC1 physically associates with PRC2 complex and regulates histone modification status of target genes. CONCLUSIONS: Frequently overexpressed linc-UBC1 physically associates with PRC2 complex, and acts as a negative prognostic factor for lymph node metastasis and survival in bladder cancer.

[878]

TÍTULO / TITLE: - Longitudinal observational cohort study about detrusor underactivity as a risk factor for bladder neck contracture after retropubic radical prostatectomy: preliminary results.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Int Urol Nephrol. 2013 Apr 17.

AUTORES / AUTHORS: - Mucciardi G; Gali A; Inferrera A; Di Benedetto A; Macchione L; Mucciardi M; Magno C
INSTITUCIÓN / INSTITUTION: - Department of Urology, University of Messina, Via Consolare Valeria, 98100, Messina, Italy.
RESUMEN / SUMMARY: - OBJECTIVES: To evaluate the association between preoperative detrusor underactivity (DU) and symptomatic bladder neck contracture (BNC) in patients undergoing radical retropubic prostatectomy (RRP), in order to identify a possible new risk factor in the etiopathogenic mechanisms of BNC after RRP. METHODS: A total of 100 prostate cancer patients underwent RRP after preoperative complete urodynamic examination. Detrusor contractility was evaluated by bladder contractility index (BCI), power at maximum flow (WF-Qmax), and maximum velocity of detrusorial contraction (MVDC). Follow-up included uroflowmetry with bladder post-voiding volume evaluation at 3 and 6 months after surgery and repeated urodynamic examination at 12 months. Statistical evaluation was performed using the Student's t test (P < 0.01). RESULTS: The mean patient age was 65.6 +/- 5.4 years, and pathological stage ranged from T2a to T2c. A total of 40 patients (40 %) presented normal detrusor contractility, 47 (47 %) mild DU, and 13 (13 %) severe DU. Detrusor overactivity (DO) was observed in 12 patients (12 %), small cystometric capacity in 10 (10 %), low compliance in 16 (16 %), DO plus DU (mild or severe) in 6 (6 %), and DO plus small cystometric capacity together with low compliance in 5 (5 %). Normal urodynamics were observed in 38 patients (38 %). Overall BNC incidence was 12. All patients with BNC presented preoperative DU; none presented DO or low bladder compliance. DU
severity and BNC occurrence were significantly correlated (P < 0.01) for all 3 urodynamic parameters (BCI, WF-Qmax, and MVDC). CONCLUSIONS: We identify DU as a possible novel risk factor for BNC formation after radical prostatectomy that may contribute to its development.

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[879]
**TÍTULO / TITLE:** - Computed tomography based renal parenchyma volume measurements prior to renal tumor surgery are predictive of postoperative renal function.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Kunzel B; Small W; Goodman M; Pattaras J; Master V; Ogan K

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Emory University School of Medicine, Atlanta, Georgia 30322, USA.

**RESUMEN / SUMMARY:** - INTRODUCTION: To determine whether preoperative computed tomography (CT) based renal parenchymal volume (RPV) measurements would be predictive of postoperative chronic kidney disease (CKD). MATERIALS AND METHODS: From 2005 to 2010, 189 patients with preoperative CT imaging performed at Emory University Hospital underwent renal tumor surgery. Preoperative and postoperative renal function was determined by estimating glomerular filtration rate (GFR) using standard Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) equations. Preoperative CT measured RPV was calculated to determine association of predicted preserved renal parenchyma with postoperative renal function and the development of CKD (GFR < 60 mL/min/1.73 m2). RESULTS: For the entire cohort, radical nephrectomy (RN), lower preoperative GFR, and volume of kidney without tumor were associated with the development of CKD (p = < 0.05). If the non-tumor bearing kidney constituted >/= 50% of the total bilateral preoperative RPV, then risks of developing CKD were decreased. In patients treated with partial nephrectomy (PN) or ablation, total bilateral preoperative RPV measurements predicted postoperative renal function (CKD >/= 3 versus CKD < 3) to a significant degree (p < 0.001). CONCLUSIONS: Preoperative CT based RPV measurements are independently associated with the development of CKD in patients undergoing renal tumor surgery. This provides urologists with another tool in the assessment of patients with renal tumors.

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[880]
**TÍTULO / TITLE:** - Hormonal therapy with external radiation therapy for metastatic spinal cord compression from newly diagnosed prostate cancer.

651
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

- Enlace al texto completo (gratuito o de pago) 1007/s00776-013-0409-y

**AUTORES / AUTHORS:** Kato S; Hozumi T; Yamakawa K; Higashikawa A; Goto T; Shinohara M; Kondo T

**INSTITUCIÓN / INSTITUTION:** Department of Orthopaedic Surgery and Musculoskeletal Oncology, Tokyo Metropolitan Komagome Hospital, 3-18-22 Honkomagome, Bunkyo-ku, Tokyo, 113-8677, Japan, skatou-tky@umin.org.

**RESUMEN / SUMMARY:** BACKGROUND: Although hormonal therapy is effective for treatment of prostate cancer, its effect in the treatment of metastatic spinal cord compression (MSCC) has not been established. The objective of this study was to clarify the efficacy of conservative treatment of MSCC-induced paralysis resulting from prostate cancer for patients without a previous treatment history. METHODS: We reviewed data from 38 patients with MSCC-induced paralysis from newly diagnosed prostate cancer who presented to our service between 1984 and 2010. Conservative treatment consisted of hormonal therapy with external radiation therapy (ERT). Patient demographic data, treatment details, involved spine MRI images, complications, and the course of neurologic recovery were investigated. RESULTS: Twenty-five patients were treated conservatively. Mean follow-up period was 36.8 months. Sixteen patients (two with Frankel B, 14 with Frankel C) were unable to walk at initial presentation. After initiating conservative treatment, 75 % (12 of 16) of these patients regained the ability to walk within 1 month, 88 % (14 in 16) did so within 3 months, and all non-ambulatory patients did so within 6 months. No one had morbid complications. Four patients who did not regain the ability to walk at 1 month were found to have progressed to paraplegia rapidly, and tended to have severe compression as visualized on MRI, with a delay in the start of treatment in comparison with those who did so within 1 month (21.0 vs. 7.8 days). CONCLUSIONS: Hormonal therapy associated with ERT is an important option for treatment of MSCC resulting from newly diagnosed prostate cancer.

**TÍTULO / TITLE:** Transcriptome profiling of mice testes following low dose irradiation.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

- Enlace al texto completo (gratuito o de pago) 1186/1477-7827-11-50

**AUTORES / AUTHORS:** Belling KC; Tanaka M; Dalgaard MD; Nielsen JE; Nielsen HB; Brunak S; Almstrup K; Jeffers H

**RESUMEN / SUMMARY:** BACKGROUND: Radiotherapy is used routinely to treat testicular cancer. Testicular cells vary in radio-sensitivity and the aim of this...
study was to investigate cellular and molecular changes caused by low dose irradiation of mice testis and to identify transcripts from different cell types in the adult testis. METHODS: Transcriptome profiling was performed on total RNA from testes sampled at various time points (n = 17) after 1 Gy of irradiation. Transcripts displaying large overall expression changes during the time series, but small expression changes between neighbouring time points were selected for further analysis. These transcripts were separated into clusters and their cellular origin was determined. Immunohistochemistry and in silico quantification was further used to study cellular changes post-irradiation (pi). RESULTS: We identified a subset of transcripts (n = 988) where changes in expression pi can be explained by changes in cellularity. We separated the transcripts into five unique clusters that we associated with spermatogonia, spermatocytes, early spermatids, late spermatids and somatic cells, respectively. Transcripts in the somatic cell cluster showed large changes in expression pi, mainly caused by changes in cellularity. Further investigations revealed that the low dose irradiation seemed to cause Leydig cell hyperplasia, which contributed to the detected expression changes in the somatic cell cluster. CONCLUSIONS: The five clusters represent gene expression in distinct cell types of the adult testis. We observed large expression changes in the somatic cell profile, which mainly could be attributed to changes in cellularity, but hyperplasia of Leydig cells may also play a role. We speculate that the possible hyperplasia may be caused by lower testosterone production and inadequate inhibin signalling due to missing germ cells.
induced migration and metastasis. MATERIALS AND METHODS: The expression and localization of CX3CR1 in RCC cell lines were assessed by immunofluorescence analysis. The migration of cancer cells was examined by wound healing and transwell migration assay. The expression level of CX3CR1 and FKN in 78 CCRCC individual samples, 16 normal kidney cortex tissue samples, and 16 cases of metastatic lesions of CCRCC were evaluated using immunohistochemical analysis on tissue microarray. The signal pathway of functional FKN was analyzed by the use of the western-blotting method and inhibitory migration assay. RESULTS: CX3CR1 was expressed in human RCC cell lines, and only membrane positive cells were responsible for FKN-induced cell migration. Extracellular signal-related kinases (ERK1/2) and phosphatidylinositide 3 kinase/Akt (PI3K/Akt) were each activated upon soluble FKN stimulation in a time-dependent manner, whereas blockades of MEK, PI3K, and G proteins prevented FKN-mediated cellular migration. Furthermore, CCRCC tissue microarray immunohistochemistry data revealed a clear association of strong CX3CR1 expression with tumor metastasis and poor prognosis. CONCLUSIONS: CX3CR1 expression is associated with the process of cellular migration in vitro and tumor metastasis of CCRCC in vivo. Both clinical and molecular cellular evidence suggest that CX3CR1 is a potential marker and therapeutic target for CCRCC prognostic prediction and treatment.

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estimated by the Kaplan-Meier method. The univariate and multivariable forward-stepwise Cox proportional hazards regression were applied to analyze the survival outcomes. RESULTS: The mean (SD) follow-up was 59.2 +/- 44.3 months, and the mean (SD) age of the entire cohort population was 68.3 +/- 8.3 years. The cancer-specific survival rates were 58.7 and 47.7 % at 5 and 10 years, respectively. Considering both node-positive and node-negative patients, those with at least 14 LNs removed and those submitted to extended or super-extended PLND experienced significantly higher cancer-specific survival at both univariate and multivariable analysis. CONCLUSIONS: Patients undergoing a more extended pelvic lymph node dissection, both in terms of number of LN removed and in terms of template of dissection, will experience a better cancer-specific survival. Our data support a potential role of lymphadenectomy on cancer outcome.
demonstrated that PSA density (p = 0.015) and percentage of cancer in biopsy material (p = 0.028) are the most significant predictors. INTERPRETATION: Our results demonstrate that PSA density and the percentage of cancer in biopsy cores are significant predictors for prostate cancer unilaterality and should be considered for the selection of hemiablative focal therapy candidates.

[885]

TÍTULO / TITLE: - The Value of “Liver Windows” Settings in the Detection of Small Renal Cell Carcinomas on Unenhanced Computed Tomography.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Sahi K; Jackson S; Wiebe E; Armstrong G; Winters S; Moore R; Low G
INSTITUCIÓN / INSTITUTION: - Department of Radiology and Diagnostic Imaging, University of Alberta Hospital, Edmonton, Alberta, Canada.
RESUMEN / SUMMARY: - OBJECTIVE: To assess if “liver window” settings improve the conspicuity of small renal cell carcinomas (RCC). METHODS: Patients were analysed from our institution’s pathology-confirmed RCC database that included the following: (1) stage T1a RCCs, (2) an unenhanced computed tomography (CT) abdomen performed <= 6 months before histologic diagnosis, and (3) age >/= 17 years. Patients with multiple tumours, prior nephrectomy, von Hippel-Lindau disease, and polycystic kidney disease were excluded. The unenhanced CT was analysed, and the tumour locations were confirmed by using corresponding contrast-enhanced CT or magnetic resonance imaging studies. Representative single-slice axial, coronal, and sagittal unenhanced CT images were acquired in “soft tissue windows” (width, 400 Hounsfield unit (HU); level, 40 HU) and liver windows (width, 150 HU; level, 88 HU). In addition, single-slice axial, coronal, and sagittal unenhanced CT images of nontumourous renal tissue (obtained from the same cases) were acquired in soft tissue windows and liver windows. These data sets were randomized, unpaired, and were presented independently to 3 blinded radiologists for analysis. The presence or absence of suspicious findings for tumour was scored on a 5-point confidence scale. RESULTS: Eighty-three of 415 patients met the study criteria. Receiver operating characteristics (ROC) analysis, t test analysis, and kappa analysis were used. ROC analysis showed statistically superior diagnostic performance for liver windows compared with soft tissue windows (area under the curve of 0.923 vs 0.879; P = .0002). Kappa statistics showed “good” vs “moderate” agreement between readers for liver windows compared with soft tissue windows. CONCLUSION: Use of liver windows settings improves the detection of small RCCs on the unenhanced CT.
TÍTULO / TITLE: - Imatinib and prostate cancer: lessons learned from targeting the platelet-derived growth factor receptor.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Rosenberg A; Mathew P
INSTITUCIÓN / INSTITUTION: - Tufts Medical Center, Department of Hematology and Oncology, 800 Washington St, Boston, MA 02111, USA.
RESUMEN / SUMMARY: - Introduction: The platelet derived growth factor (PDGF) signaling pathway has been implicated in both epithelial and stromal mechanisms of prostate cancer progression and postulated as a target for therapy in bone metastases. Imatinib mesylate is a potent inhibitor of the platelet-derived growth factor receptor (PDGFR) and its activity has been tested in preclinical models and in Phase I and II clinical trials. Areas covered: This review summarizes the preclinical data on PDGF/PDGFR in prostate cancer, and reviews the clinical and correlative data using imatinib as a PDGFR inhibitor. Expert opinion: To date, the use of imatinib to treat men with prostate cancer has been ineffective, and PDGFR inhibition may in fact accelerate advanced forms of the disease and antagonize taxane efficacy. Given the major discordance between preclinical models and clinical experimentation, an accurate understanding of the PDGF-regulated interactions between metastatic prostate cancer and the bone micro-environment is evidently warranted. Correlations of pharmacodynamic monitoring of imatinib-induced PDGFR inhibition with progression-free and overall survival outcomes have led to the hypothesis that PDGF may function as a homeostatic factor in bone metastases. Recent laboratory studies defining PDGFR-regulated pericytes as gatekeepers of metastases may relate to these clinical observations.

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TÍTULO / TITLE: - Urinary prostate-specific antigen: predictor of benign prostatic hyperplasia progression?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Pejcic TP; Tulic CDz; Lalic NV; Glisic BD; Ignjatovic SD; Markovic BB; Hadzi-Djokic JB
INSTITUCIÓN / INSTITUTION: - Clinical Center of Serbia, Urological Clinic, Belgrade, Serbia.
RESUMEN / SUMMARY: - INTRODUCTION: Urinary prostate-specific antigen (uPSA) can be used as additional parameter of benign prostatic hyperplasia (BPH) progression. MATERIALS AND METHODS: From January 2001 to December 2011, uPSA was determined in 265 patients with benign prostate. Based on total prostate volume (TPV), the patients with benign prostate were divided in two groups: TPV < 31 mL and TPV >/= 31 mL. Additional three groups were formed upon MTOPS study criteria: non-progressive BPH group (TPV < 31 mL, PSA < 1.6 ng/mL, age < 62 yrs), intermediate group (one, or two parameters (TPV, PSA, age) increased) and progressive BPH group (TPV >/= 31 mL, PSA >/= 1.6 ng/mL, age >/= 62 yrs). RESULTS: Average uPSA values in the groups TPV < 31 mL and TPV >/= 31 mL were 119.3 +/- 124.5 and 255.5 +/- 204.9 ng/mL, respectively and they were significantly different (p < 0.0001). Average uPSA values in the non-progressive BPH group, intermediate group and progressive BPH group were 86.8 +/- 82.4 ng/mL, 166.6 +/- 164.9 ng/mL and 274.9 +/- 208.3 ng/mL, respectively and they were significantly different (p < 0.0001). The level of uPSA correlated significantly with TPV (r = 0.32, p < 0.0001). The cut off uPSA level of 150 ng/mL discriminates the patients with non-progressive BPH and progressive BPH with specificity of 0.83 and sensitivity of 0.67. CONCLUSION: The level of uPSA reflects prostatic hormonal activity and correlates with TPV, PSA and age. uPSA level >/= 150 ng/mL can be used as additional predictive parameter of BPH progression.

[888]
TÍTULO / TITLE: - Percutaneous renal biopsy may aid management of small renal masses on active surveillance.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Raman JD
INSTITUCIÓN / INSTITUTION: - Department of Urology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania 17036, USA.

[889]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.jfma.2013.04.001
BACKGROUND/PURPOSE: There is relatively little literature on prevalence of chronic kidney disease (CKD) prior to surgery in patients with upper urinary tract urothelial carcinoma (UTUC). We evaluated the prevalence and clinical associated factors of baseline CKD in patients with UTUC. MATERIALS AND METHODS: There were 785 patients with a pathologic diagnosis of UTUC from January 2002 to December 2011 who were analyzed in this study. Estimated glomerular filtration rate (eGFR) was calculated by re-expressed Modification of Diet in Renal Disease (MDRD) formulas for the Chinese population. A multivariate logistic regression was performed to evaluate the odds ratios (ORs) for CKD stage 3 or higher in UTUCs after data differences were tested. RESULTS: The prevalence of CKD in UTUCs presenting at our hospital was 58.6% and 70.8% in the group age 70 years and older. Older age [per year increased; OR = 1.050; 95% confidence interval (CI): 1.034-1.067], lower tumor stage (T stage; per stage increased; OR = 0.666; 95% CI: 0.544-0.816), higher tumor grade (per grade increased; OR = 1.392; 95% CI: 1.004-1.930) and the main tumor locating in the pelvis (ureter as reference; OR = 0.648; 95% CI: 0.475-0.885) were independently associated with decreased kidney function in the multivariate logistic regression. The use of serum creatinine (Scr) only to evaluate the renal function would ignore a large proportion of patients suffering from CKD stage 3 in UTUCs, especially in those older than 70 years (39.3% vs. 54.1%, p = 0.022). CONCLUSION: We demonstrated a high prevalence (58.6%) of CKD in patients with UTUC, particularly in the group older than 70 years (70.8%). Older age, lower T stage, higher tumor grade, and the main tumor locating in pelvis (ureter as reference) were independently associated with CKD in UTUCs.

[890]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1007/s00259-013-2385-z

AUTORES / AUTHORS: - Reske SN; Winter G; Baur B; Machulla HJ; Kull T
INSTITUCIÓN / INSTITUTION: - Klinik fur Nuklearmedizin, Universitat Ulm, Ulm, Germany, sven.reske@uniklinik-ulm.de.

[891]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ••Enlace al texto completo (gratuito o de pago) 1007/s00259-013-2386- y
AUTORES / AUTHORS: - Afshar-Oromieh A; Malcher A; Eder M; Eisenhut M; Linhart HG; Hadaschik BA; Holland-Letz T; Giesel FL; Kratochwil C; Haufe S; Haberkorn U; Zechmann CM
INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, University Hospital of Heidelberg, Im Neuenheimer Feld 400, 69120, Heidelberg, Germany, ali.afshar@med.uni-heidelberg.de.

[892]
TÍTULO / TITLE: - One-stage laparoscopic procedure for a patient with bilateral colorectal tumours and renal carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Fazzin M; Dellachiesa L; Resta G; Bandi M; Marino S; Anania G
RESUMEN / SUMMARY: - We describe a case of a patient with synchronous bilateral colorectal tumours and renal carcinoma who underwent one-stage laparoscopic surgery procedure with right transperitoneal nephrectomy, right hemicolecctiony and sigmoidectomy. One-stage laparoscopic procedure can be used safely and successfully for a patient with multiple primary tumours.

[893]
TÍTULO / TITLE: - Primary synovial sarcoma of the kidney with unusual follow up findings.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Pereira E Silva R; Leitao T; Correia L; Martins F; Palma Dos Reis J; Lopes T
INSTITUCIÓN / INSTITUTION: - Department of Urology, Centro Hospitalar Lisboa Norte, EPE, Hospital de Santa Maria, Lisbon, Portugal.

RESUMEN / SUMMARY: - We present a case report of a 17-year-old patient with a large renal mass that was detected on a computed tomography scan during investigation for secondary hypertension. Radical nephrectomy was performed and the morphologic and immunocytochemical findings were compatible with a diagnosis of monophasic synovial sarcoma of the kidney. A cytogenetic search for t(X;18) translocation was performed, which was negative. The patient underwent an ifosfamide-based chemotherapy regimen. During follow up, a positron emission tomography scan showed increased 18F-fluorodeoxyglucose metabolism at the right femur. Although cancer cells were expected in the biopsy specimen, only fibrous dysplasia of the bone was found. The patient was disease free at his 29 month follow up check up.

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[TÍTULO / TITLE: - Primary testicular leiomyosarcoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Bostanci Y; Ozden E; Akdeniz E; Kazzazi A; Kandemir B; Yakupoglu YK; Djavan B
INSTITUCIÓN / INSTITUTION: - Department of Urology, New York University School of Medicine, New York, New York 19916, USA.
RESUMEN / SUMMARY: - Primary testicular leiomyosarcoma is an extremely rare tumor, and, to the best of our knowledge, only 20 cases in adults have been reported in the literature to date. Herein, we present a case of a 68-year-old man who complained of left scrotal swelling for 2 months. Radiological examination revealed a left testicular tumor with no metastases to other organs. A left inguinal orchiectomy was carried out and histopathologic examination revealed an intratesticular leiomyosarcoma. The patient was treated successfully by orchiectomy and received no adjuvant therapy. During follow up until 12 months after surgery, there has been no recurrence or metastases of the disease.

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[TÍTULO / TITLE: - Perineural invasion and TRUS findings are complementary in predicting prostate cancer biology.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Martinez CH; Williams AK; Chin JL; Stitt L; Izawa JI
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada.
RESUMEN / SUMMARY: - INTRODUCTION: Clinical variables with more accuracy to predict biologically insignificant prostate cancer are needed. We evaluated the combination of transrectal ultrasound-guided biopsy of the prostate (TRUSBx) pathologic and radiologic findings in their ability to predict the biologic potential of each prostate cancer. MATERIALS AND METHODS: A total of 1043 consecutive patients who underwent TRUSBx were reviewed. Using pathologic criteria, patients with prostate cancer (n = 529) and those treated with radical prostatectomy (RP) (n = 147) were grouped as: “insignificant” (Gleason score <= 6, prostate-specific antigen (PSA) density <= 0.15 ng/ml, tumor in <= 50% of any single core, and < 33% positive cores) and “significant” prostate cancer. TRUSBx imaging and pathology results were compared with the RP specimen to identify factors predictive of “insignificant” prostate cancer. RESULTS: TRUSBx pathology results demonstrated perineural invasion in 36.4% of “significant” versus 5.4% of “insignificant” prostate cancers (p < 0.01) and pathologic invasion of periprostatic tissue in 7% of significant versus 0% of insignificant prostate cancers (p < 0.01). TRUS findings concerning for neoplasia were associated with significant tumors (p < 0.01). Multivariable analysis demonstrated perineural invasion in the biopsy specimen (p = 0.03), PSA density (p = 0.02) and maximum tumor volume of any core (p = 0.02) were independently predictive of a significant prostate cancer. CONCLUSIONS: TRUS findings concerning for measurable tumor and perineural invasion in TRUSBx specimens appear to be complementary to Epstein’s pathologic criteria and should be considered to aid in the determination whether a prostate cancer is organ-confined and more likely to be biologically insignificant.

[896]
TÍTULO / TITLE: - Explosive growth of a renal tumor during active surveillance.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Uhlman MA; Pate SC; Brown JA
INSTITUCIÓN / INSTITUTION: - University of Iowa, Iowa City 52242-1089, USA.
RESUMEN / SUMMARY: - The incidence of small renal masses (<= 4 cm) has increased over the past three decades. Partial nephrectomy remains the standard for treatment of such lesions, but increased attention is being given to patients who may benefit from active surveillance, given the low risk of metastatic spread and traditionally slow growth rates. Patients with significant comorbidities and the elderly are often considered optimal candidates for surveillance. We present an 86-year-old female undergoing active surveillance for a 1.4 cm lesion that grew in diameter approximately 0.5 cm per year over 3 years, followed by explosive growth to 7 cm in diameter with a retrohepatic inferior vena cava (IVC) thrombus over the subsequent 13 months.
TÍTULO / TITLE: - Recent Less-invasive Circulatory Monitoring during Renal Transplantation.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Soga T; Kawahito S; Oi R; Kakuta N; Katayama T; Wakamatsu N; Takaishi K; Yamaguchi K; Izaki H; Kanayama HO; Kitahata H; Oshita S

INSTITUCIÓN / INSTITUTION: - Department of Anesthesiology, Tokushima University Hospital.

RESUMEN / SUMMARY: - For anesthetic management during renal transplantation, it is necessary to maintain the blood flow and function of the transplanted kidney by performing massive fluid management and stabilizing blood pressure. We report anesthetic management for renal transplantation with a less-invasive circulatory monitoring system (Edwards Life Sciences Co., Ltd., Irvine, California, U.S.A.). In November 2010, renal transplantation was started in our hospital, and performed in 6 patients. In the first patient, fluid/circulatory management was conducted by connecting a standard arterial line and a standard central venous (CV) line. In the second patient, a FloTrac™ system and a standard CV line were used. In the third patient, a standard arterial line and a PreSep™ CV Oximetry Catheter were used. In the fourth and fifth patients, a FloTrac™ and a PreSep™ were used. In the latest patient, FloTrac™ and PreSep™ were connected to an EV1000™ Clinical Platform for fluid/circulatory management. The establishment of high-visibility monitors was useful for evaluating the condition and confirming the effects. As there are marked changes in hemodynamics, the CV pressure, which has been used as a parameter of fluid management, is not reliable in renal failure patients with a high incidence of cardiovascular complications. Advances in noninvasive circulatory monitoring with dynamic indices may improve the safety of anesthetic management during renal transplantation. J. Med. Invest. 60: 159-163, February, 2013.

TÍTULO / TITLE: - Association of micropapillary urothelial carcinoma of the bladder and BK viruria in kidney transplant recipients.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1111/tid.12072
INTRODUCTION: BK virus (BKV) is an ubiquitous human polyomavirus that establishes latency in urothelium. BKV is known to reactivate in immunosuppressed individuals, and is an increasingly important cause of nephropathy and graft loss in kidney transplant recipients. Animal studies have demonstrated BKV has a potential role as a tumor virus. However, its role in precipitating or facilitating oncogenesis in humans is still debated.

REPORT: We report 2 cases of aggressive micropapillary urothelial carcinoma of the bladder in kidney transplant recipients with persistent BK viruria and preserved graft function. RESULTS: In both cases, polyomavirus immunohistochemistry performed on the tumor specimens was strongly positive, and limited to the malignant tissue. BKV DNA, viral protein 1, and large T antigen mRNA were detected in the tumor; however, no viral particles were seen on electron microscopy. CONCLUSION: In one of the cases, BKV integration into the host genome was identified, leading to the truncation of the major viral capsid gene. This finding raises the concern that persisting BK viruria may be a risk factor for this aggressive form of bladder cancer. Further studies to determine screening and management strategies are required.

Should you get a PSA test? The latest thinking on this controversial screening.

Metabolomic imaging of prostate cancer with magnetic resonance spectroscopy and mass spectrometry.

Metabolomic imaging of prostate cancer (PCa) aims to improve in vivo imaging capability so that PCa tumors can be localized
noninvasively to guide biopsy and evaluated for aggressiveness prior to prostatectomy, as well as to assess and monitor PCa growth in patients with asymptomatic PCa newly diagnosed by biopsy. Metabolomics studies global variations of metabolites with which malignancy conditions can be evaluated by profiling the entire measurable metabolome, instead of focusing only on certain metabolites or isolated metabolic pathways. At present, PCa metabolomics is mainly studied by magnetic resonance spectroscopy (MRS) and mass spectrometry (MS). With MRS imaging, the anatomic image, obtained from magnetic resonance imaging, is mapped with values of disease condition-specific metabolomic profiles calculated from MRS of each location. For example, imaging of removed whole prostates has demonstrated the ability of metabolomic profiles to differentiate cancerous foci from histologically benign regions. Additionally, MS metabolomic imaging of prostate biopsies has uncovered metabolomic expression patterns that could discriminate between PCa and benign tissue. Metabolomic imaging offers the potential to identify cancer lesions to guide prostate biopsy and evaluate PCa aggressiveness noninvasively in vivo, or ex vivo to increase the power of pathology analysis. Potentially, this imaging ability could be applied not only to PCa, but also to different tissues and organs to evaluate other human malignancies and metabolic diseases.

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[901]
TITULO / TITLE: - Diffusion pattern of low dose rate brachytherapy for prostate cancer in Japan.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
    ●●Enlace al texto completo (gratuito o de pago) 1111/cas.12168
AUTORES / AUTHORS: - Nakamura K; Ohga S; Yorozu A; Dokiya T; Saito S; Yamanaka H
INSTITUCIÓN / INSTITUTION: - Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.
RESUMEN / SUMMARY: - Permanent implant brachytherapy for prostate cancer using iodine-125 seeds was adopted in Japan in 2003. Here, we report on the diffusion pattern of this treatment in Japan since 2003. We examined the annual numbers of prostate cancer patients per hospital in Japan, who were treated with iodine-125 seed implant brachytherapy with or without external beam radiation therapy between 2003 and 2011. The hospitals were excluded from the count if brachytherapy was begun in a hospital within the given year, and thus was only available for part of the year. In 2004, 269 patients were treated by brachytherapy at only two hospitals. However, the numbers increased rapidly. A total of 1412 patients were treated at 23 hospitals in 2005, 2783 patients were treated at 83 hospitals in 2008, and 3793 patients were treated at
109 hospitals in 2011. The mean/median numbers of patients treated per hospital were 61.4/42 in 2005, 33.5/25 in 2008, and 35.0/24 in 2011. The number of hospitals where 24 or fewer patients were treated in a year increased. On the other hand, the number of hospitals with a volume of >48 patients per year was stable. Because a relationship between provider volume and outcomes following oncological procedures was shown, a careful evaluation of the effectiveness of permanent implant brachytherapy for prostate cancer is needed.

[902]

TÍTULO / TITLE: - NF-kappaB2/p52 induces resistance to Enzalutamide in Prostate Cancer: Role of androgen receptor and its variants.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Nadiminty N; Tummala R; Liu C; Yang J; Lou W; Evans CP; Gao AC

INSTITUCIÓN / INSTITUTION: - 1Urology and Cancer Center, University of California at Davis.

RESUMEN / SUMMARY: - Resistance of prostate cancer (CaP) cells to the next generation anti-androgen, Enzalutamide, may be mediated by a multitude of survival signaling pathways. In this study we tested whether increased expression of NF-kappaB2/p52 induces CaP cell resistance to Enzalutamide and whether this response is mediated by aberrant androgen receptor (AR) activation and AR splice variant production. LNCaP cells stably expressing NF-kappaB2/p52 exhibited higher survival rates compared to controls when treated with Enzalutamide. C4-2B and CWR22Rv1 cells chronically treated with Enzalutamide were found to express higher levels of NF-kappaB2/p52. Downregulation of NF-kappaB2/p52 in CWR22Rv1 cells chronically treated with Enzalutamide rendered them more sensitive to cell growth inhibition by Enzalutamide. Analysis of the expression levels of AR splice variants by qRT-PCR and Western blotting revealed that LNCaP cells expressing p52 exhibit higher expression of AR splice variants. Downregulation of expression of NF-kappaB2/p52 in VCaP and CWR22Rv1 cells by shRNA abolished expression of splice variants. Downregulation of expression of either full length AR or the splice variant AR-V7 led to an increase in sensitivity of CaP cells to Enzalutamide. These results collectively demonstrate that resistance to Enzalutamide may be mediated by NF-kappaB2/p52 via activation of AR and its splice variants.
[903]
TITULO / TITLE: - Nephroblastomas in adults.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ben Mrad M; Aissi S; Zarraa S; Laabidi S; Boussen H

[904]
TITULO / TITLE: - Vitamin e and prostate cancer: a case in point to explore the placebo.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hoskote SS; Nadkarni GN; Fried ED
INSTITUCIÓN / INSTITUTION: - Department of Medicine, St. Luke’s-Roosevelt Hospital Center, Columbia University College of Physicians and Surgeons, New York, NY.

[905]
TITULO / TITLE: - Prevalence and predictors of cancer specific distress in men with a family history of prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - McDowell ME; Occhipinti S; Gardiner RA; Chambers SK
INSTITUCIÓN / INSTITUTION: - Griffith Health Institute, School of Applied Psychology, Griffith University, Brisbane, Queensland, Australia.
RESUMEN / SUMMARY: - OBJECTIVE: To examine prevalence and predictors of cancer-specific distress in undiagnosed men with and without a family history of prostate cancer, and to examine the contribution of perceptions of an affected relative’s cancer experience on the distress of unaffected male relatives.
METHODS: Men with a first degree relative with prostate cancer (n = 207) and men without a family history (n = 239) from Australia completed a Computer Assisted Telephone Interview. Participants completed the Prostate Cancer Anxiety Subscale of the Memorial Anxiety Scale for Prostate Cancer, measures of perceived risk, and socio-demographic information. Men with a family history provided details about their family history (number of relatives diagnosed with and dead from prostate cancer, relationship to affected relative, months since diagnosis) and reported their perceptions of their affected relative’s prostate cancer experience including perceptions of threat related to the relative’s
diagnosis and perceived treatment phase and prognosis. RESULTS: Cancer-specific distress was low for all men and there was no significant difference in the distress experienced by men with and without a family history. Regression analyses showed that for all men, cancer-specific distress increased with urinary symptoms and decreased in those with higher education and in older participants. For men with a family history, having a relative who died from prostate cancer and perceiving greater threat from a relative’s diagnosis was associated with greater cancer-specific distress. CONCLUSIONS: Interventions would benefit from examining appraisals of familial risk and examining prospective assessments of distress in the unaffected male relatives of men with prostate cancer over the course of the cancer trajectory. Copyright © 2013 John Wiley & Sons, Ltd.

[906]
TÍTULO / TITLE: - Changes in S-PSA after transurethral resection of prostate and its correlation to postoperative outcome.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1007/s11255-013-0474-3
AUTORES / AUTHORS: - Pahwa M; Pahwa M; Pahwa AR; Girotra M; Chawla A; Sharma A
INSTITUCIÓN / INSTITUTION: - Sir Ganga Ram Hospital, New Delhi, India, drmrinalpahwa@gmail.com.
RESUMEN / SUMMARY: - PURPOSE: Although different factors may affect prostate-specific antigen (PSA) reduction after transurethral resection of prostate, an approximate 70 % decrease from baseline is expected. We hereby undertook a prospective study to analyze changes in serum PSA (S-PSA) after transurethral resection of the prostate (TURP) and its correlation with the residual prostatic weight and clinical symptom score improvement. METHODS: Seventy patients who underwent TURP for bladder outlet obstruction were included in the study. Patient’s evaluation included history, International Prostate Symptom Score (IPSS), S-PSA, Qmax, post-void residual urine and prostate size. On follow-up, trans-rectal ultrasonography, S-PSA and IPSS score were calculated. Patients were analyzed in three groups based on the amount of tissue resected: less than 40, 40-60 and more than 60 % tissue resected. RESULTS: Preoperative prostate size, IPSS, Qmax and S-PSA were 62.56 ml, 23.84, 11.68 ml/sec and 3.3 ng/ml. There was a significant decrease in the IPSS score, prostate size and S-PSA levels after TURP in all the three groups. There was a significant positive correlation of the amount of tissue resected with change in S-PSA levels, change in IPSS score and postoperative IPSS score. Reduction in IPSS score significantly correlated with patient’s
satisfaction. CONCLUSIONS: The amount of tissue resected in TURP has a direct bearing on the S-PSA levels, change in symptom score and residual prostate volume. It is the percentage change in IPSS score and not the absolute value of IPSS, which has a direct bearing with the patient satisfaction and with the amount of tissue resected. Percentage fall in S-PSA by 70 % was found to be predictor of more than 60 % resection.

[907]
**TÍTULO / TITLE:** - Functional and molecular imaging of localized and recurrent prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Grant K; Lindenberg ML; Shebel H; Pang Y; Agarwal HK; Bernardo M; Kurdziel KA; Turkbey B; Choyke PL

**INSTITUCIÓN / INSTITUTION:** - Molecular Imaging Program, National Cancer Institute, NIH, Bethesda, MD, USA.

**RESUMEN / SUMMARY:** - Prostate cancer is the most common malignancy among American men. Imaging of localized and recurrent prostate cancer is challenging since conventional imaging techniques are limited. New imaging techniques such as multiparametric MRI and PET with targeted tracers have been investigated extensively in the last decade. As a result, the role of novel imaging techniques for the detection of localized and recurrent prostate cancer has recently expanded. In this review, novel functional and molecular imaging techniques used in the management of localized and recurrent prostate cancer are discussed.

[908]
**TÍTULO / TITLE:** - Secondary Circulating Prostate Cells Predict Biochemical Failure in Prostate Cancer Patients after Radical Prostatectomy and without Evidence of Disease.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Murray NP; Reyes E; Orellana N; Fuentealba C; Badinez L; Olivares R; Porcell J; Duenas R

**INSTITUCIÓN / INSTITUTION:** - Division of Medicine, Hospital de Carabineros de Chile, Simon Bolivar 2200, Nunoa, 7770199 Santiago, Chile; Instituto de Bio-Oncologia, Avenida Salvador 95, Oficina 95, Providencia, 7500710 Santiago,
RESUMEN / SUMMARY: - Introduction. Aunque el 90% del cáncer de próstata se considera localizado, el 20%-30% de los pacientes experimentará fracaso bioquímico (BF), definido como un nivel de PSA >0.2 ng/mL, después de la prostatectomía radical (RP). La presencia de células circulantes de próstata (CPCs) en hombres sin evidencia de BF puede ser útil para predecir a los pacientes en riesgo de BF. Describimos la frecuencia de CPCs detectada después de RP, relación con los parámetros clinicopatológicos, y asociación con el fracaso bioquímico. Métodos y Pacientes. Se tomaron muestras de sangre seriadas durante el seguimiento después de RP, se obtuvieron células mononucleares mediante centrífugación diferencial, y se identificaron CPCs utilizando inmunocitoquímica estándar usando anticuerpos monoclonales antí-PSA. La edad, el estadio patológico (confinado al órgano, no confinado), el grado patológico, el estado del margen (positivo, negativo), la extensión extracapsular, la infección perineural, vascular y linfática (positiva, negativa) se compararon con la presencia/ausencia de CPCs y con y sin fracaso bioquímico. Métodos de Kaplan Meier se utilizaron para comparar la supervivencia libre de fracaso bioquímico no ajustada de los pacientes con y sin CPCs. Resultados. 114 hombres participaron, y las CPCs secundarias se detectaron con mayor frecuencia en pacientes con margen positivo, extensión extracapsular y vascular e infiltración linfática y estaban asociadas con BF independientemente de estos parámetros clinicopatológicos, y con un tiempo de BF más corto. Conclusiones. Las CPCs secundarias son un factor de riesgo independiente asociado con un aumento de BF en hombres con un PSA <0.2 ng/mL después de la prostatectomía radical, pero no determinan si la recurrencia es debido a enfermedad local o sistémica. Estos resultados requieren estudios más grandes para confirmar los hallazgos.

[909]
TÍTULO / TITLE: - Optimizing outcomes for octogenarians with invasive bladder cancer: One size does not fit all.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Resnick MJ; Chang SS
INSTITUCIÓN / INSTITUTION: - Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, TN, USA.
matthew.resnick@vanderbilt.edu

[910]
TÍTULO / TITLE: - A rare case of retroperitoneal malignant Triton tumor invading renal vein and small intestine.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
INTRODUCTION: Malignant Triton tumor is a very rare malignant peripheral nerve sheath tumor with rhabdomyosarcomatous differentiation. Most of those tumors occur in patients with von Recklinghausen’s disease or as a late complication of irradiation and commonly seen in the head, neck, extremities and trunk. CASE REPORT: We reported retroperitoneal malignant Triton tumor in a 57-year-old female patient. Skin lesions were not present, and there was no family history of neurofibromatosis or previous irradiation. The presented case is one of a few recorded in the specialized literature that occurs in the retroperitoneal space in sporadic form. In this case, tumor consisted of a multilobular mass was in close relation with the abdominal aorta and inferior vena cava and involved the renal vein with gross invasion of the small intestine. The patient underwent total resection of the tumor and left nephrectomy was performed. The small intestine 10 cm in length was also resected and end-to-end anastomosis was conducted. The postoperative course was uneventful and the patient was discharged from the hospital ten days after the surgery. CONCLUSION: Diagnostically, it is crucial to recognize this uncommon histological variant because malignant Triton tumor has a worse prognosis than classic malignant peripheral nerve sheath tumor does. The use of the immunohistochemistry is essential in making the correct diagnosis. Only appropriate pathological evaluation supported by immunostaining with S-100 protein and desmin confirmed the diagnosis. Aggressive surgical management treatment improves the prognosis of such cases with adjuvant radiotherapy.
INTRODUCTION: Multiple genetic studies have confirmed association of 8q24 variants with susceptibility to prostate cancer (CaP). However, the risk conferred in men living in Russia is unknown.

MATERIALS AND METHODS: In this work we studied the association of rs6983267, rs10090154, and rs1447295 single nucleotide polymorphisms (SNPs) with a risk of CaP development in men of Caucasoid descent living in the Siberian region of Russia. Three 8q24 SNPs were genotyped by real-time polymerase chain reaction in histologically confirmed CaP “cases” (n = 392) and clinically evaluated “controls” (n = 344). To evaluate the SNP effects on CaP susceptibility, odds ratio (OR) and confidence interval (CI) 95% were calculated. Allele and genotype frequencies in the groups were compared using logistic regression; differences were considered statistically significant if P<0.05. RESULTS: We showed statistically significant association of the A allele of rs1447295 (OR [CI 95%] = 1.96 [1.37-2.81], P<0.0001) and the T allele of rs10090154 (OR [CI 95%] = 2.14 [1.41-3.26], P<0.0001) with CaP. The T-A rs10090154 to rs1447295 haplotype was also associated with CaP (OR [CI 95%] = 2.47 [1.59-3.85], P<0.0001). There was no significant association with the T allele of rs6983267: OR [CI 95%] = 0.9 [0.73-1.11], P> 0.05.

CONCLUSION: Thus, our investigation confirms the role of chromosomal region 8q24 in the development of CaP in the Russian population.

TÍTULO / TITLE: Long non-coding RNA GAS5 regulates apoptosis in prostate cancer cell lines.
GAS5 on prostate cell survival has not been determined. To address this question, prostate cell lines were transfected with GAS5-encoding plasmids or GAS5 siRNAs, and cell survival was assessed. Basal apoptosis increased, and cell survival decreased, after transfection of 22Rv1 cells with plasmids encoding GAS5 transcripts, including mature GAS5 lncRNA alone. Similar effects were observed in PC-3 cells. In stable clones of 22Rv1, cell death correlated strongly with cellular GAS5 levels. Induction of 22Rv1 cell death by UV-C irradiation and chemotherapeutic drugs was augmented in cells transiently transfected with GAS5 constructs, and attenuated following down-regulation of GAS5 expression. Again, in these experiments, cell death was strongly correlated with cellular GAS5 levels. Thus, GAS5 promotes the apoptosis of prostate cells, and exonic sequence, i.e. GAS5 lncRNA, is sufficient to mediate this activity. Abnormally low levels of GAS5 expression may therefore reduce the effectiveness of chemotherapeutic agents. Although several lncRNAs have recently been shown to control cell survival, this is the first report of a death-promoting lncRNA in prostate cells.

[913]

**TÍTULO / TITLE:** - Independent prognostic factors for initial intravesical recurrence after laparoscopic nephroureterectomy for upper urinary tract urothelial carcinoma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Liu Y; Lu J; Hong K; Huang Y; Ma L

**INSTITUCIÓN / INSTITUTION:** - Urology Department, Peking University Third hospital, Haidian District, Beijing, China.

**RESUMEN / SUMMARY:** - OBJECTIVE: To elucidate clinicopathologic independent prognostic factors for intravesical recurrence after laparoscopic nephroureterectomy for primary upper urinary tract urothelial carcinoma (UUT-UC). METHODS AND MATERIALS: This study included 212 consecutive patients clinically diagnosed as localized UUT-UC and treated by retroperitoneal laparoscopic nephroureterectomy between January 2002 and October 2010, after exclusion of those with a previous or concurrent history of bladder cancer. The clinicopathologic features, risk factors, and intravesical recurrence-free survival were analyzed using the Kaplan-Meier method. Univariate and multivariate analyses by Cox proportional hazards regression model was used to identify independent risk factors for intravesical tumor recurrence. RESULTS: Of the patients, 64/212 (30.2%) developed subsequent intravesical recurrence during a median follow-up period of 39 months (range 7-78 months). Among
them, 56/64 (87.5%) developed recurrent bladder cancer within 2 years after the surgery for UUT-UC, and the median interval between surgery and intravesical recurrence was 14 months (range 7-51 months). Multifocal tumors, renal insufficiency, and immunosuppression were determined as risk factors for intravesical recurrence by univariate analysis. However, by multivariate analyses, multifocality (hazard ratio = 2.060, P = 0.006) and immunosuppression (hazard ratio = 1.915, P = 0.037) were identified as independent predictors for the development of recurrent bladder cancer.

CONCLUSIONS: The incidence of intravesical recurrence after laparoscopic nephroureterectomy for UUT-UC is high, and most subsequent bladder cancers recur within 2 years after surgery. Tumor multifocality and immunosuppression are significant independent risk factors in developing initial intravesical recurrence after laparoscopic surgery for primary UUT-UC.

[914]
TÍTULO / TITLE: - Choline PET/CT for imaging prostate cancer: an update.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kitajima K; Murphy RC; Nathan MA
INSTITUCIÓN / INSTITUTION: - Department of Radiology, Kobe University Graduate School of Medicine, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe, 650-0017, Japan, kitajima@med.kobe-u.ac.jp.
RESUMEN / SUMMARY: - Whole-body positron emission tomography/computed tomography (PET/CT) with [11C]- and [18F]-labeled choline derivates has emerged as a promising molecular imaging modality for the evaluation of prostate cancer. 11C- and 18F-choline PET/CT are used successfully for restaging prostate cancer in patients with biochemical recurrence of disease after definitive therapy, especially when the serum prostate-specific antigen level is >1.0 ng/mL. 11C- and 18F-choline PET/CT have more limited roles for the initial staging of prostate cancer and for the detection of tiny lymph node metastases due to the low spatial resolution inherent to PET. Overall, these modalities are most useful in patients with a high pre-test suspicion of metastatic disease. The following is a review of the current clinical roles of 11C- and 18F-choline PET/CT in the management of prostate cancer.

[915]
TÍTULO / TITLE: - Preoperative decision making for renal cell carcinoma: Cystic morphology in cross-sectional imaging might predict lower malignant potential.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
OBJECTIVES: Several histologic studies showed more favorable oncologic outcome for renal cell carcinoma (RCC) with cystic change. However, there is no prognostic tool to judge on cystic RCC preoperatively. We hypothesized, that cystic morphology in cross-sectional imaging predicts lower malignant potential. MATERIALS AND METHODS: From our prospectively conducted oncologic database, we identified 825 patients who underwent surgery for malignant renal tumors between 2001 and 2010. In 348 cases (42%), adequate imaging was available for an independent review by 2 radiologists. We excluded recurrent and synchronous bilateral RCC, familial syndromes, collecting duct carcinoma, and metastases of other origin. For the resulting 319 patients, we compared clinical, pathologic, and survival outcomes. RESULTS: Median age was 63 (19-88) years and 220 (69%) patients were male. Median follow-up was 1.7 (0-9.8) years. Of 319 renal masses, 277 (86.8%) were solid and 42 (13.2%) were cystic. In cystic RCC, median tumor diameter was lower (3cm vs. 4cm, P = 0.002) and nephron-sparing surgery was more frequent (69% vs. 41.5%, P = 0.002). None of the patients with cystic RCC and 56 (20.2%) with solid RCC had synchronous systemic disease (P = 0.001). The nuclear grade of cystic RCC was more favorable (P = 0.002). Patients with cystic RCC showed better overall (P = 0.049) and cancer-specific survival (P = 0.027). In a multivariate model, only synchronous metastases, positive R status, and greater tumor diameter were independent risk factors (P<= 0.03). CONCLUSIONS: We report the first study to show that cystic morphology in cross-sectional imaging might predict RCC with a lower malignant potential. This insight could allow less invasive treatment strategies in selected patients.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Savoy RM; Ghosh PM

INSTITUCIÓN / INSTITUTION: - Departments of Urology Biochemistry and Molecular Medicine, University of California Davis, Sacramento, California, USA
VA Northern California Health Care System, Sacramento, California, USA.

RESUMEN / SUMMARY: - A new paper by Tawadros et al. in Endocrine-Related Cancer demonstrates a link between macrophage migration inhibitory factor and neuroendocrine differentiation in prostate cancer. This paper may have implications in explaining the effect of prostatitis and chronic inflammation on the development of aggressive prostate cancer.
[918]

TÍTULO / TITLE: - PET/MR in prostate cancer: technical aspects and potential diagnostic value.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratis o de pago) 10.1007/s00259-013-2445-4
AUTORES / AUTHORS: - Souvatzoglou M; Eiber M; Martinez-Moeller A; Fürst S; Holzapfel K; Maurer T; Ziegler S; Nekolla S; Schwaiger M; Beer AJ
INSTITUCIÓN / INSTITUTION: - Klinik fur Nuklearmedizin, Technischen Universität Munchen, Ismaninger Str. 22, 81675, Munchen, Germany, msouvatz@yahoo.de.
RESUMEN / SUMMARY: - PET/MR is a new multimodal imaging technique that is expected to improve diagnostic performance of imaging in conditions in which assessment of changes in soft tissue is important such as prostate cancer. Despite substantial changes in PET technology compared to PET/CT, initial studies have demonstrated that integrated PET/MR provides comparable image quality to that of PET/CT, retaining PET quantification efficacy. In this review we briefly describe technological changes compared to PET/CT that made integrated PET/MR possible, propose acquisition protocols for evaluation of prostate cancer with this new multimodal approach, present initial results concerning the application of PET/MR in prostate cancer, and outline the potential for further clinical applications, focusing on potential incremental value compared to present diagnostic performance.

[919]

- CASTELLANO -

TÍTULO / TITLE: Verlauf von Spatnebenwirkungen am Rektum und an der Harnblase nach MRI-gestützter Brachytherapie des Zervixkarzinoms.
TÍTULO / TITLE: - Time course of late rectal- and urinary bladder side effects after MRI-guided adaptive brachytherapy for cervical cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratis o de pago) 10.1007/s00066-013-0365-7
AUTORES / AUTHORS: - Georg P; Boni A; Ghabuous A; Goldner G; Schmid MP; Georg D; Potter R; Dorr W
INSTITUCIÓN / INSTITUTION: - Department of Radiooncology, Medical University Vienna/AKH Wien, Wahringer Gurtel 18-20, 1090, Vienna, Austria, petra.georg@akhwien.at.
RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: To analyze the time course of late rectal- and urinary bladder complications after brachytherapy for cervical cancer and to compare the incidence- and prevalence rates thereof. PATIENTS AND METHODS: A total of 225 patients were treated with external-beam radiotherapy (EBRT) and magnetic resonance imaging (MRI)-guided brachytherapy with or without chemotherapy. Late side effects were assessed prospectively using the Late Effects in Normal Tissue-Subjective, Objective, Management and Analytic (LENT/SOMA) scale. The parameters analyzed were time to onset, duration, actuarial incidence- (occurrence of new side effects during a defined time period) and prevalence rates (side effects existing at a defined time point). RESULTS: Median follow up was 44 months. Side effects (grade 1-4) in rectum and bladder were present in 31 and 49 patients, 14 and 27 months (mean time to onset) after treatment, respectively. All rectal and 76 % of bladder side effects occurred within 3 years after radiotherapy. Mean duration of rectal events was 19 months; 81 % resolved within 3 years of their initial diagnosis. Mean duration of bladder side effects was 20 months; 61 % resolved within 3 years. The 3- and 5-year actuarial complication rates were 16 and 19 % in rectum and 18 and 28 % in bladder, respectively. The corresponding prevalence rates were 9 and 2 % (rectum) and 18 and 21 % (bladder), respectively. CONCLUSION: Late side effects after cervical cancer radiotherapy are partially reversible, but their time course is organ-dependent. The combined presentation of incidence- and prevalence rates provides the most comprehensive information.

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TÍTULO / TITLE: - The Prostate Cancer Patient Had Higher C-Reactive Protein Than BPH Patient.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kim Y; Jeon Y; Lee H; Lee D; Shim B
INSTITUCIÓN / INSTITUTION: - Department of Urology, Ewha Womans University School of Medicine, Seoul, Korea.
RESUMEN / SUMMARY: - PURPOSE: C-reactive protein (CRP) is a general marker for inflammation and it has been associated with prostate cancer. We hypothesized that a correlation may exist between CRP and prostate cancer in patients undergoing transrectal biopsy of the prostate because of rising prostate-specific antigen (PSA) levels. MATERIALS AND METHODS: From January 2009 to March 2012, we retrospectively reviewed 710 patients who visited our urology department and were diagnosed as having a PSA value over 4.0 ng/mL. Patients with acute infections, rheumatoid arthritis, gout, asthma,
chronic lung disease, myocardial infarction, or apoplexy and those who had taken nonsteroidal anti-inflammatory drugs were exempted from the research because these variables could have impacted CRP. After we applied the exclusion criteria, we selected 63 patients with prostate cancer and 140 patients with benign prostatic hyperplasia (BPH). RESULTS: A total of 203 patients were observed: 140 patients had BPH, and 63 patients had prostate cancer. Prostate cancer patients were divided into two groups by tumor-node-metastasis classification. The patients below T2 were group A, and those above T3 were group B. The natural logarithm of C-reactive protein (lnCRP) differed between the BPH group and the prostate cancer group. The lnCRP also differed between the BPH group and prostate cancer groups A and B (p<0.05). CONCLUSIONS: The serum CRP level of the prostate cancer group was higher than that of the BPH group. Inflammation may be correlated with prostate cancer according to the serum CRP level.

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[921]
TÍTULO / TITLE: - Oncology: The Role of Partial Nephrectomy in Wilms Tumor.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratis o de pago) 1007/s11934-013-0330-0
AUTORES / AUTHORS: - Harel M; Makari JH; Ferrer FA Jr
INSTITUCIÓN / INSTITUTION: - Connecticut Children’s Medical Center, Hartford, CT, USA, MHarel@ccmckids.org.
RESUMEN / SUMMARY: - Wilms tumor represents the most common pediatric renal malignancy and the fourth most common childhood cancer overall. Overall survival from Wilms tumor has increased to over 90 % secondary to multidisciplinary therapy and multi-institutional cooperative group trials. Recent therapeutic focus has shifted to reduction in treatment morbidity and renal preservation while maintaining the high survival rates. Partial nephrectomy is an integral component of the multimodal treatment protocols for Wilms tumor patients with bilateral disease, solitary kidney, or predisposing syndromes. Recent consideration has been given to utilization of nephron sparing surgery (NSS) in carefully selected patients with nonsyndromic unilateral Wilms tumor. While long-term, prospective data in this subgroup of patients is not yet available, case series demonstrate comparable oncologic outcomes after partial versus radical nephrectomy. The relative rarity of Wilms tumor, especially those amenable to upfront partial nephrectomy, presents a challenge to conducting controlled trials.

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[922]
**TÍTULO / TITLE:** - Review on Targeted Treatment of Patients with Advanced-Stage Renal Cell Carcinoma: A Medical Oncologist’s Perspective.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Tanriverdi O

**INSTITUCIÓN / INSTITUTION:** - Department of Medical Oncology, Mugla Sitki Kocman University Education and Research Hospital, Mugla, Turkey E-mail: ozgurtanriverdi@hotmail.com.

**RESUMEN / SUMMARY:** - Renal cell carcinomas make up 3% of all cancers and one in four patients is metastatic at time of diagnosis. This cancer is one of the most resistant to cytotoxic chemotherapy. Studies have shown that the efficiency of interferon-alpha and/or interleukin-2 based immune therapies is limited in patients with metastatic renal cell carcinoma but latest advances in molecular biology and genetic science have resulted in better understanding of its biology. Tumor angiogenesis, tumor proliferation and metastasis develop by the activation of signal message pathways playing a role in the development of renal cell carcinomas. Better definition of these pathways has caused an increase in preclinical and clinical studies into target directed treatment of renal cell carcinoma. Many recent studies have shown that numerous anti-angiogenic agents have marked clinical activity. In this article, the focus is on general characteristics of molecular pathways playing a major role in renal cell carcinoma, reviewing clinical information on agents used in the target directed treatment of metastatic lesions.

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[923]

**TÍTULO / TITLE:** - New paradigms in microtubule-mediated endocrine signaling in prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Mistry SJ; Oh WK

**INSTITUCIÓN / INSTITUTION:** - Corresponding Authors: Sucharita J. Mistry, Division of Hematology-Oncology, Icahn School of Medicine at Mount Sinai, New York, NY 10029. Sucharita.mistry@mssm.edu.

**RESUMEN / SUMMARY:** - Metastatic prostate cancer has limited therapeutic options and has remained a major clinical challenge. Historically, prostate cancer has been widely recognized as a chemotherapy-resistant disease. However, clinical studies with anti-microtubule agents over the past decade have shown important efficacy in improving survival in patients with advanced disease. The favorable outcomes with microtubule-targeted agents have thus
rekindled interest in such therapies for the clinical management of prostate cancer. Microtubules are dynamic polymers of tubulin molecules that play diverse roles within the cell. The dynamic property of microtubules is responsible for forming the bipolar mitotic apparatus, the mitotic spindle, that functions to precisely segregate the chromosomes during cell division. Thus, owing to the pivotal role that they play in the orchestration of mitotic events, microtubules provide excellent targets for anti-cancer therapy. Recent evidence also suggests that microtubules play a crucial role in the regulation of endocrine signaling pathways. Interestingly, microtubule-targeted agents such as taxanes not only inhibit cell division but also impair endocrine receptor signaling in prostate cancer. Herein, we provide an overview of the current status of microtubule-targeted therapies that are used in the treatment of prostate cancer and discuss novel mechanisms by which such therapies modulate endocrine signaling in prostate cancer. We also address the emerging roles of microtubule regulatory proteins in prostate carcinogenesis that could serve as attractive targets for prostate cancer therapy and might also serve as predictive biomarkers to identify patients who may benefit from endocrine and/or chemotherapy. This may have important implications in designing mechanism-based and targeted-therapeutic strategies for prostate cancer. Mol Cancer Ther; 12(5): 555-66. ©2013 AACR.

[924] TÍTULO / TITLE: - Prognostic Factors of Survival for Patients With Metastatic Renal Cell Carcinoma With Brain Metastases Treated With Targeted Therapy: Results From the International Metastatic Renal Cell Carcinoma Database Consortium.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Vickers MM; Al-Harbi H; Choueiri TK; Kollmannsberger C; North S; Mackenzie M; Knox JJ; Rini BI; Heng DY
INSTITUCIÓN / INSTITUTION: - Department of Oncology, Tom Baker Cancer Centre, Calgary, Alberta, Canada. Electronic address: michael.vickers@albertahealthservices.ca.
RESUMEN / SUMMARY: - BACKGROUND: The outcomes and prognosis of patients with brain metastases from advanced renal cell carcinoma (RCC) are not well characterized in the targeted-therapy era. METHODS: Data from patients with metastatic RCC (mRCC) and brain metastases treated with targeted therapy were collected through the International Metastatic Renal Cell Carcinoma Database Consortium from 7 cancer centers. RESULTS: Overall, 106 (15%) of 705 patients with mRCC had brain metastases. Forty-seven
patients had brain metastases at the start of first-line anti-vascular endothelial growth factor therapy, and the rest developed metastases during follow-up. Of the patients with brain metastases, 12%, 42% and 29% were in the favorable, intermediate, and poor prognosis groups, respectively, per the Heng criteria. Ninety percent had cerebral metastases, 17% had cerebellar metastases, 37% had a Karnofsky performance status (KPS) <80%, and 80% had neurologic symptoms at presentation. The median largest size and number of brain metastases was 1.8 cm (range, 0.2-6.6 cm) and one (range, 1 to innumerable), respectively. The patients were treated with sunitinib (n = 77), sorafenib (n = 23), bevacizumab (n = 5), and temsirolimus (n = 1). Local disease treatment included whole brain radiotherapy (81%), stereotactic radiosurgery (25%), and neurosurgery (25%). On multivariable analysis, KPS < 80%, diagnosis to treatment with targeted therapy <1 year, and a higher number of brain metastases (>4) was associated with worse survival from the time of diagnosis with brain metastases. CONCLUSIONS: Patients with brain metastases from RCC are unlikely to be in the favorable risk group. KPS at the start of therapy, diagnosis to treatment time, and the number of brain metastases are prognostic factors for overall survival.

[925]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Liang S; Cuevas G; Tizani S; Salas T; Liu H; Li B; Habib SL
RESUMEN / SUMMARY: - BACKGROUND: Deficiency in tuberin results in activation the mTOR pathway and leads to accumulation of cell matrix proteins. The mechanisms by which tuberin regulates fibrosis in kidney angiomyolipomas (AMLs) of tuberous sclerosis patients are not fully known. METHOD: In the present study, we investigated the potential role of tuberin/mTOR pathway in the regulation of cell fibrosis in AML cells and kidney tumor tissue from tuberous sclerosis complex (TSC) patients. RESULTS: AML cells treated with rapamycin shows a significant decrease in mRNA and protein expression as well as in promoter transcriptional activity of alpha-smooth muscle actin (alpha-SMA) compared to untreated cells. In addition, cells treated with rapamycin significantly decreased the protein expression of the transcription factor YY1. Rapamycin treatment also results in the redistribution of YY1 from the nucleus to cytoplasm in AML cells. Moreover, cells treated with rapamycin resulted in a significant reduce of binding of YY1 to the alphaSMA promoter element in nuclear extracts of AML cells. Kidney angiomyolipoma tissues from TSC patients showed lower levels of tuberin and higher levels of phospho-p70S6K
that resulted in higher levels of mRNA and protein of alphaSMA expression compared to control kidney tissues. In addition, most of the alpha-SMA staining was identified in the smooth muscle cells of AML tissues. YY1 was also significantly increased in tumor tissue of AMLs compared to control kidney tissue suggesting that YY1 plays a major role in the regulation of alphaSMA.

CONCLUSIONS: These data comprise the first report to provide one mechanism whereby rapamycin might inhibit the cell fibrosis in kidney tumor of TSC patients.

[926]

**TÍTULO / TITLE:** The PPI network and cluster ONE analysis to explain the mechanism of bladder cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Wan FC; Cui YP; Wu JT; Wang JM; Z Liu Q; Gao ZL

**INSTITUCIÓN / INSTITUTION:** Department of Urology, Yantai Yuhuangding Hospital, Yantai, Shandong Province, China.

**RESUMEN / SUMMARY:** BACKGROUND: Bladder cancer is a common cancer worldwide whose incidence continues to increase. It is estimated that there are 261,000 cases of bladder cancer resulting in 115,000 deaths worldwide. AIM: Although some studies can be initiated using small local tissue collections, high quality collection of fresh tissues from new clinical trials will be crucial for proper evaluation of associations with clinical outcome. For superficial bladder cancer, identification of tumors that will progress has long been perceived as a potential application of genetic studies. MATERIALS AND METHODS: In our study, we constructed the Protein-Protein Interactions (PPI) network using the Cytoscape and detected some network modeling clusters. In addition, we enriched GO categories among these genes in the first cluster and detected a pathway i.e. Spliceosome (hsa03040). Most Gene Ontology (GO) categories and Spliceosome were closely to RNA splicing and cellular macromolecular complex (CMC) assembly, which indicates that the mutation of RNA splicing and CMC assembly maybe important factors causing bladder cancer. RESULTS: In our study, these clusters of GO:0034622, GO:0006397 and GO:0034621 in bladder cancer belong to cellular macromolecular complex assembly, which may play an important role in the occurrence of cancer cells. CONCLUSIONS: It is a great significance for the detection and treatment of bladder cancer to understand the mechanism of RNA splicing and CMC assembly.

[927]

**TÍTULO / TITLE:** Current mouse and cell models in prostate cancer research.
Mouse models of prostate cancer (PCa) are critical for understanding the biology of PCa initiation, progression, and treatment modalities. Here, we summarize recent advances in PCa mouse models that led to new insights into specific gene functions in PCa. For example, the study of transgenic mice with TMPRSS2/ERG, an androgen regulated fusion protein, revealed its role in developing PCa precursor lesions, prostate intraepithelial neoplasia (PIN) but not sufficient for PCa development. Double deficiency of Pten and Smad4 leads to a high incidence of metastatic PCa. Targeted deletion of Pten in castration-resistant Nkx3-1-expressing cells (CARNs) results in rapid carcinoma formation after androgen-mediated regeneration, indicating progenitor cells with luminal characteristics can play a role in initiation of PCa. Transgenic mice with activated oncogenes, growth factors, and steroid hormone receptors or inactivated tumor suppressors continue to provide insight for disease progression from initiation to metastasis. Further development of new PCa models with spatial and temporal regulation of candidate gene expression will likely enhance our understanding of the complex events that lead to PCa initiation and progression, thereby invoking novel strategies to combat this common disease in men.

[928]

Unmet needs in the prediction and detection of metastases in prostate cancer.

The therapeutic landscape for the treatment of advanced prostate cancer is rapidly evolving, especially for those patients with metastatic castration-resistant prostate cancer (CPRC). Despite advances in therapy options, the diagnostic landscape has remained relatively static, with few guidelines or reviews addressing the optimal timing or methodology for the
radiographic detection of metastatic disease. Given recent reports indicating a substantial proportion of patients with CRPC thought to be nonmetastatic (M0) are in fact metastatic (M1), there is now a clear opportunity and need for improvement in detection practices. Herein, we discuss the current status of predicting the presence of metastatic disease, with a particular emphasis on the detection of the M0 to M1 transition. In addition, we review current data on newer imaging technologies that are changing the way metastases are detected. Whether earlier detection of metastatic disease will ultimately improve patient outcomes is unknown, but given that the therapeutic options for those with metastatic and nonmetastatic CRPC vary, there are considerable implications of how and when metastases are detected.

[929]

TÍTULO / TITLE: - Role of F-choline PET/CT in suspicion of relapse following definitive radiotherapy for prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 10.1007/s00259-013-2433-8

AUTORES / AUTHORS: - Chondrogiannis S; Marzola MC; Ferretti A; Maffione AM; Rampin L; Grassetto G; Nanni C; Colletti PM; Rubello D

INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, PET/CT Centre, “Santa Maria della Misericordia” Hospital, Via Tre Martiri 140, 45100, Rovigo, Italy.

RESUMEN / SUMMARY: - PURPOSE: The aims of the study were (a) to evaluate the diagnostic role, by means of positive detection rate (PDR), of 18F-choline (CH) positron emission tomography (PET)/CT in patients with prostate cancer treated with radiotherapy, with curative intent, and suspicion of relapse during follow-up, (b) to correlate the PDR with trigger prostate-specific antigen (PSA), (c) to investigate the possible influence of androgen deprivation therapy (ADT) at the time of scan on PDR and (d) to assess distribution of metastatic spread.

METHODS: 18F-CH PET/CT exams from 46 consecutive patients (mean age 71.3 years, range 51-84 years) with prostate cancer (mean Gleason score 6.4, range 5-8) previously treated by definitive radiotherapy and with suspicion of relapse with negative or inconclusive conventional imaging were retrospectively evaluated. Of the 46 patients, 12 were treated with brachytherapy and 34 with external beam radiation therapy. Twenty-three patients were under ADT at the time of the examination. Trigger PSA was measured within 1 month before the exam (mean value 6.5 ng/ml, range 1.1-49.4 ng/ml). Patients were subdivided into four groups according to their PSA level: 1.0 < PSA <= 2.0 ng/ml (11 patients), 2.0 < PSA <= 4.0 ng/ml (16 patients), 4.0 < PSA <= 6.0 ng/ml (9 patients) and PSA > 6.0 ng/ml (10 patients). Correlation between ADT and PDR
was investigated as well as between PSA and distribution of metastatic spread.

**RESULTS:** The overall PDR of 18F-CH PET/CT was 80.4 % (37/46 patients), increasing with the increase of trigger PSA. PDR of 18F-CH PET/CT is not influenced by ADT (p = 0.710) even if PET performed under ADT demonstrated an overall higher PDR (82.6 %). The majority of the patients (59 %, 22/37 patients) showed local relapse only, confined to the prostatic bed; 22 % of the PET/CT-positive patients (8/37 patients) showed distant relapse only (bone localizations in all of them), while the remaining 19 % (7/37 patients) showed both local and distant (lymph node and bone) spread. **CONCLUSION:** 18F-CH PET/CT showed a high overall detection rate (80 %), proportional to the trigger PSA (both for local and distant relapse) not influenced by ADT. 18F-CH PET/CT is proposed as a first-line imaging procedure in restaging prostate cancer patients primarily treated with radiotherapy.

[TÍTULO / TITLE: - Pretargeted immuno-PET and radioimmunotherapy of prostate cancer with an anti-TROP-2 x anti-HSG bispecific antibody.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - van Rij CM; Lutje S; Frielink C; Sharkey RM; Goldenberg DM; Franssen GM; McBride WJ; Rossi EA; Oyen WJ; Boerman OC
INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, k.vanrij@akf.umcn.nl.
RESUMEN / SUMMARY: - PURPOSE: TF12 is a trivalent bispecific antibody that consists of two anti-TROP-2 Fab fragments and one anti-histamine-succinyl-glycine (HSG) Fab fragment. The TROP-2 antigen is found in many epithelial cancers, including prostate cancer (PC), and therefore this bispecific antibody could be suitable for pretargeting in this cancer. In this study, the characteristics and the potential for pretargeted radioimmunoimaging and radioimmunotherapy with TF12 and the radiolabeled di-HSG peptide IMP288 in mice with human PC were investigated. METHODS: The optimal TF12 protein dose, IMP288 peptide dose, and dose interval for PC targeting were assessed in nude mice with s.c. PC3 xenografts. Immuno-positron emission tomography (PET)/CT was performed using TF12/68Ga-IMP288 at optimized conditions. The potential of pretargeted radioimmunotherapy (PRIT) using the TF12 pretargeted 177Lu-IMP288 was determined. RESULTS: TF12 and 111In-IMP288 showed high and fast accumulation in the tumor [20.4 +/- 0.6 %ID/g at 1 h post-injection (p.i.)] at optimized conditions, despite the internalizing properties of TF12. The potential for PRIT was shown by retention of 50 % of the 111In-IMP288 in the tumor at
48 h p.i. One cycle of treatment with TF12 and 177Lu-IMP288 showed significant improvement of survival compared to treatment with 177Lu-IMP288 alone (90 vs. 67 days, p < 0.0001) with no renal or hematological toxicity. CONCLUSION: TROP-2-expressing PC can be pretargeted efficiently with TF12, with very rapid uptake of the radiolabeled hapten-peptide, IMP288, sensitive immuno-PET, and effective therapy.

[931]
TÍTULO / TITLE: Identification, prioritization and evaluation of glycoproteins for aggressive prostate cancer using quantitative glycoproteomics and antibody-based assays on tissue specimens.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Chen J; Xi J; Tian Y; Bova GS; Zhang H
INSTITUCIÓN / INSTITUTION: Department of Pathology, Johns Hopkins University, Baltimore, MD, USA.
RESUMEN / SUMMARY: Prostate cancer is highly heterogeneous in nature; while the majority of cases are clinically insignificant, some cases are lethal. Currently, there are no reliable screening methods for aggressive prostate cancer. Since most established serum and urine biomarkers are glycoproteins secreted or leaked from the diseased tissue, the current study seeks to identify glycoprotein markers specific to aggressive prostate cancer using tissue specimens. With LC-MS/MS glycoproteomic analysis, we identified 350 glycopeptides with 17 being altered in aggressive prostate cancer. ELISA assays were developed/purchased to evaluate 4 candidates, i.e. cartilage oligomeric matrix protein (COMP), periostin, membrane primary amin oxidase (VAP-1) and cathepsin L, in independent tissue sets. In agreement with the proteomic analysis, we found that COMP and periostin expressions were significantly increased in aggressive prostate tumors while VAP-1 expression was significantly decreased in aggressive tumor. In addition, the expression of these proteins in prostate metastases also follows the same pattern observed in the proteomic analysis. This study provides a workflow for biomarker discovery, prioritization and evaluation of aggressive prostate cancer markers using tissue specimens. Our data suggest increase in COMP and periostin and decrease in VAP-1 expression in the prostate may be associated with aggressive prostate cancer. This article is protected by copyright. All rights reserved.

[932]
TÍTULO / TITLE: Percutaneous nephrostomy for ureteric obstruction due to advanced pelvic malignancy: have we got the balance right?
PURPOSE: The optimal management of patients with ureteric obstruction in advanced pelvic malignancy is unclear. Effective judgment is required to decide which patients would benefit most from decompression of the urinary tract. The objective of our study was to assess survival and complication rates post-percutaneous nephrostomy (PCN) in patients with ureteric obstruction due to advanced pelvic malignancy.

METHODS: A detailed retrospective case review of all patients who underwent PCN for ureteric obstruction due to pelvic malignancy in one calendar year was conducted to assess indication, survival time, length of stay post-procedure and complications. RESULTS: Thirty-six nephrostomies were performed on 22 patients with prostate cancer being the commonest primary (55%). Renal failure was the commonest mode of presentation (56%). Eight patients (36%) presented without a prior diagnosis of cancer. All PCNs except one were initially technically successful, and 56% of renal units were able to be antegradely stented and rendered free of nephrostomy. Median survival post-nephrostomy was 78 days (range 4-1,137), with the subset of bladder cancer patients having the poorest survival. Dislodgement of the nephrostomy tube was the most common troublesome complication which led to the greatest morbidity, sometimes requiring repeat nephrostomy insertion. Patients stayed for a median of 23 (range 3-89) days in hospital, which amounted to 29% of their remaining lifetime spent in hospital. CONCLUSIONS: Although effective in improving renal function, PCN is a procedure not without associated morbidity and does not always prolong survival. Therefore, the decision to decompress an obstructed kidney with advanced pelvic malignancy should not be taken lightly. We recommend that such cases be discussed in a multidisciplinary setting, and a decision is taken only after a full informed discussion involving patients and their relatives.
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[934]

TÍTULO / TITLE: - Minimally invasive management with holmium laser in total urinary tract calculi.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Zhang X; Yu J; Yang R
INSTITUCIÓN / INSTITUTION: - Department of Urology, the Affiliated Hospital of Shanghai JiaoTong University, Shanghai Sixth People’s Hospital, Shanghai, China.
RESUMEN / SUMMARY: - Abstract Objective: The purpose of this article was to study the management of total urinary tract calculi using holmium laser minimally invasive techniques. Background data: It is rare for patients to present kidney stones, ureteral stones, and bladder stones simultaneously, and their treatment is considered to be complicated and difficult, specifically by minimally invasive techniques. Methods: We collected seven cases of total urinary tract calculi from May 2007 to September 2012. Three cases were unilateral, and the others were bilateral. All of the cases presented calculus in the bladder, ureter, and kidney, which were secondary to the long-term indwelling double J stent or lower urinary obstruction. Results: Extracorporeal shock-wave lithotripsy (SWL) was administered first, followed by the operation. For patients with bilateral calculi, at one stage, ureteroscopic lithotripsy (URL) with holmium laser was performed in all four cases to remove the bladder and bilateral ureter stones. Then, all patients underwent percutaneous nephrolithotomy (PCNL) with holmium procedures to address the bilateral kidney and upper ureter stones at the second stage. The indwelling double J stents were removed at the same time. For the patients with unilateral calculi, we performed a single operation, but it was conducted using the same treatment sequence as the bilateral procedure. The related symptoms in all cases disappeared after the operation. Re-examination showed that the stones were nearly dissolved and that renal function was recovered. Conclusions: URL with holmium laser for the bladder and ureters combined with PCNL to dissolve kidney and upper ureteral stones could be the ideal choice for the treatment of total urinary tract calculi.
Aristolochic acid (AA), a plant nephrotoxin and carcinogen, causes aristolochic acid nephropathy (AAN) and its associated urothelial malignancy, and is hypothesized to be responsible for Balkan endemic nephropathy (BEN). The major component of AA, aristolochic acid I (AAI), is the predominant compound responsible for these diseases. The reductive activation of AAI leads to the formation of covalent DNA adducts. The most abundant DNA adduct, 7-(deoxyadenosin-N6-yl)aristolactam I, causes characteristic AT-->TA transversions found in the TP53 tumor suppressor gene in tumors from AAN and BEN patients. Understanding which human enzymes are involved in AAI activation to species forming DNA adducts and/or detoxication to the AAI O-demethylated metabolite, aristolochic acid Ia (AAIa), is important in the assessment of the susceptibility to this carcinogen. This review summarizes the latest data on identifying human and rodent enzymes participating in AAI metabolism. NAD(P)H:quinone oxidoreductase (NQO1) is the most efficient cytosolic nitroreductase activating AAI in vitro and in vivo. In human hepatic microsomes, AAI is activated by cytochrome P450 1A2 (CYP1A2) and, to a lesser extent, by CYP1A1; NADPH:CYP oxidoreductase also plays a minor role. Human and rodent CYP1A1 and 1A2 are also the principal enzymes involved in oxidative detoxication of AAI to AAIa in vitro and in vivo. The orientation of AAI in the active sites of human CYP1A1/2 and NQO1 was predicted from molecular modeling and is consistent with the efficient reduction of AAI by them observed experimentally. Molecular modeling also shows why CYP1A2 plays an important role in the oxidation of AAI to AAIa.
BACKGROUND: An in vitro model was developed to understand if celecoxib could synergize with Mitomycin C (MMC), commonly used for the prevention of non-muscle invasive bladder cancer recurrence, and eventually elucidate if the mechanism of interaction involves multi drug resistance (MDR) transporters. METHODS: UMUC-3, a non COX-2 expressing bladder cancer cell line, and UMUC-3-CX, a COX-2 overexpressing transfectant, as well as 5637, a COX-2 overexpressing cell line, and 5637si-CX, a non COX-2 expressing silenced 5637 cell line, were used in the present study. The expression of COX-2 and MDR pumps (P-gp, MDR-1 and BCRP) was explored through western blot. The anti-proliferative effect of celecoxib and MMC was studied with MTT test. Three biological permeability assays (Drug Transport Experiment, Substrate Transporter Inhibition, and ATP cell depletion) were combined to study the interaction between MDR transporters and celecoxib. Finally, the ability of celecoxib to restore MMC cell accumulation was investigated. RESULTS: The anti-proliferative effect of celecoxib and MMC were investigated alone and in co-administration, in UMUC-3, UMUC-3-CX, 5637 and 5637si-CX cells. When administered alone, the effect of MMC was 8-fold greater in UMUC-3. However, co-administration of 1 μM, 5 μM, and 10 μM celecoxib and MMC caused a 2,3-fold cytotoxicity increase in UMUC-3-CX cell only. MMC cytotoxicity was not affected by celecoxib co-administration either in 5637, or in 5637si-CX cells. As a result of all finding from the permeability experiments, celecoxib was classified as P-gp unambiguous substrate: celecoxib is transported by MDR pumps and interferes with the efflux of MMC. Importantly, among all transporters, BCRP was only overexpressed in UMUC-3-CX cells, but not in 5637 and 5637si-CX. CONCLUSIONS: The UMUC-3-CX cell line resembles a more aggressive phenotype with a lower response to MMC compared to the wt counterpart. However, the administration of celecoxib in combination to MMC causes a significant and dose dependent gain of the anti-proliferative activity. This finding may be the result of a direct interaction between celecoxib and MDR transporters. Indeed, BCRP is overexpressed in UMUC-3-CX, but not in UMUC-3, 5637, and 5637si-CX, in which celecoxib is ineffective.
Following Walsh’s advances in pelvic anatomy and surgical technique to minimize intraoperative peri-prostatic trauma more than 30 years ago, open retropubic radical prostatectomy (RRP) evolved to become the gold standard treatment of localized prostate cancer, with excellent long-term survival outcomes [1*]. However, RRP is performed with great heterogeneity, even among high volume surgeons, and subtle differences in surgical technique result in clinically significant differences in recovery of urinary and sexual function. Since the initial description of robotic-assisted radical prostatectomy (RARP) in 2000 [2], and U.S. Food and Drug Administration approval shortly thereafter, RARP has been rapidly adopted and has overtaken RRP as the most popular surgical approach in the management of prostate cancer in the United States [3]. However, the surgical management of prostate cancer remains controversial. This is confounded by the idolatry of new technologies and aggressive marketing versus conservatism in embracing tradition. Herein, we review the literature to compare RRP to RARP in terms of perioperative, oncologic, and quality-of-life outcomes as well as healthcare costs. This is a particularly relevant, given the absence of randomized trials and long-term (more than 10-year) follow-up for RARP biochemical recurrence-free survival.
Current literature suggests that the standard of care for these patients is a combination approach with radiation therapy and androgen deprivation therapy. However, there remain many unresolved issues, including the role of dose-escalated radiation therapy, the additional benefit of surgery and the role of systemic therapy, both standard chemotherapeutic agents and novel agents. Furthermore, in the era of personalised medicine, additional research is needed to evaluate the role of biomarkers to better predict the risk of local and systemic relapse in this population.

[939]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Russo GI; Cimino S; Salamone C; Madonia M; Favilla V; Castelli T; Morgia G
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RESUMEN / SUMMARY: - Traditional medicine is very popular in Africa and it is considered as an alternative form of health care. Plants and vegetables used in folk and traditional medicine have gained wide acceptance as one of the main sources of prophylactic and chemopreventive drug discovery and this is due to the evidence of particular biological and biochemical characteristics of each plants extracts. The role of these compounds in urological field may be explained by the anti-inflammatory effect through interference with prostaglandin metabolism, alteration of lipid peroxidation, direct inhibition of prostate growth and moreover through an antiandrogenic or antiestrogenic effect and a decrease of the availability of sex hormone-binding globulin. Since Benign Prostatic Hyperplasia and Prostate Cancer are two of the most diffuse diseases of aging male and considering that standard medical therapy is accompanied with different side effects, the emerging use of African plants may be justified. This review takes a look at some African plants extracts properties and their relative urological application.

[940]
TÍTULO / TITLE: - Evaluation of everolimus in renal cell cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Resumen / Summary:

Introduction: The incidence of renal cell cancer (RCC) has been steadily increasing over the past decade. Advances in understanding the pathophysiology and carcinogenesis RCC have led to the development of novel therapies that target molecular pathways. Everolimus is a synthetic, orally available analogue of rapamycin that inhibits the activation of mTOR. Everolimus extended progression-free survival in RCC patients from 1.9 months (for patients receiving a placebo) to 4.9 months. Grades 3 and 4 adverse events include stomatitis, fatigue, pneumonitis, infections, asthenia, diarrhea, mucosal inflammation, dyspnea, rash, anorexia and dry skin. Grades 3 and 4 laboratory abnormalities include lymphopenia, anemia, thrombocytopenia, hyperglycemia, hypophosphatemia, hypercholesterolemia, hypertriglyceridemia, elevated creatinine, elevated alkaline phosphatase, elevated aspartate aminotransferase and elevated alanine aminotransferase. Studies have been conducted to evaluate any synergistic effect of combination therapies and continue to need to be further evaluated. Areas covered: A systematic review of medical literature for everolimus as a single agent or combination was completed using PubMed. Expert opinion: Everolimus has significant clinical benefit and is well tolerated with reversible side effects as second- or third-line therapy for treating RCC. The next phase of research for everolimus is determining patient selection based on mTOR profile utilizing skills such as proteomics and genomics.

Título / Title: The fat side of prostate cancer.

Resumen / Summary: Prostate cancer (PCa) metabolism appears to be unique in comparison with other types of solid cancers. Normal prostate cells mainly rely on glucose oxidation to provide precursors for the synthesis and secretion of citrate, resulting in an incomplete Krebs cycle and minimal oxidative phosphorylation for energy production. In contrast, during transformation, PCa
cells no longer secrete citrate and they reactivate the Krebs cycle as energy source. Moreover, primary PCas do not show increased aerobic glycolysis and therefore they are not efficiently detectable with 18F-FDG-PET. However, increased de novo lipid synthesis, strictly intertwined with deregulation in classical oncogenes and oncosuppressors, is an early event of the disease. Up-regulation and increased activity of lipogenic enzymes (including fatty acid synthase and choline kinase) occurs throughout PCa carcinogenesis and correlates with worse prognosis and poor survival. Thus, lipid precursors such as acetate and choline have been successfully used as alternative tracers for PET imaging. Lipid synthesis intermediates and FA catabolism also emerged as important players in PCa maintenance. Finally, epidemiologic studies suggested that systemic metabolic disorders including obesity, metabolic syndrome, and diabetes as well as hypercaloric and fat-rich diets might increase the risk of PCa. However, how metabolic disorders contribute to PCa development and whether dietary lipids and de novo lipids synthesized intra-tumor are differentially metabolized still remains unclear. In this review, we examine the switch in lipid metabolism supporting the development and progression of PCa and we discuss how we can exploit its lipogenic nature for therapeutic and diagnostic purposes. This article is part of a Special Issue entitled Dysregulated Lipid Metabolism in Cancer.

[942]
TÍTULO / TITLE: Prostate cancer genomics by high-throughput technologies: genome-wide association study and sequencing analysis.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Nakagawa H
INSTITUCIÓN / INSTITUTION: H Nakagawa, Laboratory for Biomarker Development, Center for Genomic Medicine, RIKEN, Tokyo, 108-8639, Japan.
RESUMEN / SUMMARY: Prostate cancer (PC) is the most common malignancy in males. It is evident that genetic factors at both germline and somatic levels play critical roles in prostate carcinogenesis. Recently, genome-wide association studies (GWAS) by high-throughput genotyping technology have identified more than 70 germline variants on various genes or chromosome loci that are significantly associated with PC susceptibility. They include multiple 8q24 loci, prostate-specific genes, and metabolism-related genes. Somatic alterations in PC genome have been explored by high-throughput sequencing technologies such as whole genome sequencing and RNA sequencing, which have identified a variety of androgen-response events and fusion transcripts represented by ETS gene fusions. Recent innovations in high-throughput genomic technologies have enabled us to analyze PC genomics more
comprehensively, more precisely, and on a larger scale in multiple ethnic
groups to increase our understanding of PC genomics and biology in germline
and somatic studies, which can ultimately lead to personalized medicine for PC
diagnosis, prevention, and therapy. However, these data indicate that the PC
genome is more complex and heterogeneous than we expected from GWAS
and sequencing analyses.

[943]
**TITULO / TITLE:** - Breast metastasis from testicular leiomyosarcoma.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)
  Epub 2013 Apr 18.
  ●●Enlace al texto Completo (gratuito o de pago) [1111/tbj.12116](#)
**AUTORES / AUTHORS:** - Kohi MP; Brasic N; Vohra P; Price ER; Joe BN
**INSTITUCIÓN / INSTITUTION:** - Department of Radiology and Biomedical Imaging,
University of California, San Francisco, California.

[944]
**TITULO / TITLE:** - Identification of drug candidate against prostate cancer from
the aspect of somatic cell reprogramming.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)
  ●●Enlace al texto Completo (gratuito o de pago) [1111/cas.12183](#)
**AUTORES / AUTHORS:** - Kosaka T; Nagamatsu G; Saito S; Oya M; Suda T;
Horimoto K
**INSTITUCIÓN / INSTITUTION:** - Department of Urology, The Sakaguchi Laboratory,
School of Medicine, Keio University, Tokyo, Japan.
**RESUMEN / SUMMARY:** - Considering the similarities between the transcriptional
programming involved in cancer progression and somatic cell reprogramming,
we tried to identify drugs that would be effective against malignant cancers. We
used the early transposon Oct4 and Sox2 enhancer (EOS) system to select
human prostate cancer (PCA) cells expressing high levels of OCT4. Patients
with metastatic castration-resistant PCA that does not respond to treatment with
docetaxel have few therapeutic options. The OCT4-expressing PCA cells
selected using the EOS system showed increased tumorigenicity and high
resistance to docetaxel, both in vitro and in vivo. By using their gene expression
data, expression signature-based prediction for compound candidates identified
an antiviral drug, ribavirin, as a conversion modulator from drug resistance to
sensitivity. Treatment of PCA cells with ribavirin decreased their resistance
against treatment with docetaxel. This indicated that ribavirin reversed the gene
expression, including that of humoral factors, in the OCT4-expressing PCA
cells selected using the EOS system. Thereby, ribavirin increased the efficacy of docetaxel for cancer cells. We propose a novel cell reprogramming approach, named drug efficacy reprogramming, as a new model for identifying candidate antitumor drugs.
Restoration of IGFBP-rP1 increases radiosensitivity and chemosensitivity in hormone-refractory human prostate cancer.

We previously reported the tumor-suppressive activity of insulin-like growth factor binding protein-related protein 1 (IGFBP-rP1) through induction of apoptosis in human prostate cancer cells. The aim of this study was to investigate the effects of IGFBP-rP1 for radiosensitivity and chemosensitivity in hormone-refractory human prostate PC-3 cancer cells. Five assays were performed using PC-3 cells transfected with IGFBP-rP1 (PC-3rP1) and control cells transfected with an empty vector (PC-3N): PC-3rP1 and PC-3N were compared by clonogenic survival assay, cell cycle analysis and apoptotic assay for radiosensitivity. The number of colonies of PC-3rP1 cells significantly decreased after 4 and 8 Gy of irradiation, compared with those of PC-3N in the clonogenic survival assay. After 16 hr irradiation at 8 Gy, the percentage of apoptotic cells significantly increased in PC-3rP1 compared with PC-3N. Growth of PC-3rP1 was significantly lower than that of PC-3N after docetaxel treatment both in vitro and in vivo. These results indicate that restoration of IGFBP-rP1 to PC-3 cells increases both their radiosensitivity and chemosensitivity.

Overexpression of CD73 in Prostate Cancer is Associated with Lymph Node Metastasis.

Prostate cancer is the most common malignancy in men in Europe and North America. At present, it is becoming an increasingly common cancer in China. CD73 (ecto-5'-nucleotidase) is a glycosylphosphatidylinositol (GPI)-linked 70-kDa cell surface enzyme. It is also broadly expressed in many types of tissues. Recent studies have showed that
CD73 is widely expressed on malignancies and is up-regulated in cancerous tissues. Consequently, we analyzed the expression of CD73 in prostate cancer tissue. The expression of the CD73 protein was evaluated by Immunohistochemistry staining in 116 tissue specimens. The expression was further examined by quantitative real-time PCR (qRT-PCR) and Western blot in the same set of patients. The intense cell membrane staining for the CD73 protein was observed. The expression of CD73 in lymph node non-metastasizing prostate cancer tissues can be seen at low levels, and is generally undetectable. RT-PCR and Western blot showed that the expression of CD73 in lymph node metastasizing prostate cancer was higher compared with non-metastasizing ones. These results suggest that CD73 could be considered as a relevant-specific target for molecular therapy of prostate cancer metastasis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Serghini M; Boussorra H; Chelly I; Karoui S; Haouet S; Boubaker J; Filali A

[950] TÍTULO / TITLE: - Impact of tumor vascularity on responsiveness to antiangiogenesis in a prostate cancer stem cell-derived tumor model.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Zhang K; Waxman DJ
INSTITUCIÓN / INSTITUTION: - Corresponding Author: David J. Waxman, Department of Biology, 5 Cummington Mall, Boston, MA 02215. diw@bu.edu.
RESUMEN / SUMMARY: - Drugs that target the tumor vasculature and inhibit angiogenesis are widely used for cancer treatment. Individual tumors show
large differences in vascularity, but it is uncertain how these differences affect responsiveness to antiangiogenesis. We investigated this question using two closely related prostate cancer models that differ markedly in tumor vascularity: PC3, which has very low vascularity, and the PC3-derived cancer stem-like cell holoclone PC3/2G7, which forms tumors with high microvessel density, high tumor blood flow, and low hypoxia compared with parental PC3 tumors. Three angiogenesis inhibitors (axitinib, sorafenib, and DC101) all induced significantly greater decreases in tumor blood flow and microvessel density in PC3/2G7 tumors compared with PC3 tumors, as well as significantly greater decreases in tumor cell proliferation and cell viability and a greater increase in apoptosis. The increased sensitivity of PC3/2G7 tumors to antiangiogenesis indicates they are less tolerant of low vascularity and suggests they become addicted to their oxygen- and nutrient-rich environment. PC3/2G7 tumors showed strong upregulation of the proangiogenic factors chemokine ligand 2 (CCL2) and VEGFA compared with PC3 tumors, which may contribute to their increased vascularity, and they have significantly lower endothelial cell pericyte coverage, which may contribute to their greater sensitivity to antiangiogenesis. Interestingly, high levels of VEGF receptor-2 were expressed on PC3 but not PC3/2G7 tumor cells, which may contribute to the growth static response of PC3 tumors to VEGF-targeted antiangiogenesis. Finally, prolonged antiangiogenic treatment led to resumption of PC3/2G7 tumor growth and neovascularization, indicating these cancer stem-like cell-derived tumors can adapt and escape from antiangiogenesis. Mol Cancer Ther; 12(5); 787-98. ©2013 AACR.

[951]
TÍTULO / TITLE: - Non hodgkin’s lymphoma presenting of the testicle.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Azzabi S; Boukhris I; Albuweiri A; Cherif E; Ben Hassine L; Kooli C; Kaouech Z; Khalfallah N

[952]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Niesser M; Harder U; Koletzko B; Peissner W
Folate catabolites p-aminobenzoylglutamate (pABG) and p-acetamidobenzoylglutamate (apABG) in human urine result from breakdown of endogenous folate pools and are potential biomarkers of folate status. There is growing interest in analysis of these non-invasive indicators of folate status, since widespread diseases such as cancer, arteriosclerosis and dementia may be linked to disturbed availability of folates. Determination of pABG and apABG in human urine is challenging due to their low urinary concentrations and due to interferences with other urinary compounds. To address these analytical difficulties, we developed an improved LC-MS/MS method with chemical derivatization for fast, selective and sensitive quantification of pABG and apABG in human urine. Forming butyl esters of urinary folate catabolites pABG and apABG improves ionization efficiency as well as enables selective chromatographic separation on standard C18 reversed-phase column material. In contrast to some previously proposed methods for folate catabolites, the new method allows precise differentiation of apABG from pABG. Partial degradation of apABG during derivatization is exactly accounted for using a second differentially labeled stable isotope internal standard. This method is highly sensitive and covers the full range of physiologically occurring concentrations (from 2 to 1000nmol/L), with volume requirements of only 80μL urine. Method performance has been validated according to widely accepted standard recommendations. Use of two stable isotope-labeled internal standards and qualifier ion monitoring for both analytes ensure correct identification and unbiased quantification. With run times of less than 2.5min per sample and cost-efficient sample preparation, this method allows exact quantitation of urinary folate catabolites pABG and apABG for large-scale non-invasive screening of folate status in clinical and epidemiological trials.
RESUMEN / SUMMARY: - BACKGROUND: Congenital adrenal hyperplasia (CAH) is an autosomal recessive condition leading to deficient cortisol with an incidence of 1/16,000. Patients with CAH typically present early with ambiguous genitalia or as an emergency with adrenal crisis. CASE: We report an atypical late presentation of a 4-year-old girl with pubertal-like symptoms and urinary incontinence, due to a persistent urogenital sinus (UGS). An early vaginoplasty was successfully performed allowing the patient to achieve continence. CONCLUSION: Literature describing the symptoms of CAH with UGS is scarce. The case is unusual in demonstrating pubertal-like symptoms and urinary incontinence due to the late presentation of a persistent UGS, highlighting the need for an open mind in assessment of children with urinary incontinence. Timing of surgery is controversial, and cases need to be considered on an individual basis.

[954]
TÍTULO / TITLE: - Intrinsic immune alterations in renal cell carcinoma and emerging immunotherapeutic approaches.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
***Enlace al texto completo (gratuito o de pago) 1517/14712598.2013.778970
AUTORES / AUTHORS: - Bockorny B; Dasanu CA
INSTITUCIÓN / INSTITUTION: - University of Connecticut, Department of Medicine, 263 Farmington Avenue, Farmington, CT 06030-1235, USA Bbockorny@resident.uchc.edu
RESUMEN / SUMMARY: - Introduction: Individuals affected by kidney cancer present a variety of immune abnormalities including cellular immune dysfunction, cytokine alterations and antigen presentation defects. On the other hand, spontaneous remissions are seen in up to 4% of renal cell carcinoma (RCC) patients and they are thought to occur via immune mechanisms. Areas covered: The authors comprehensively review the immune abnormalities in RCC patient and describe the kidney cancer immunotherapy candidates that are most advanced in their clinical development. Most relevant publications were identified through searching the PubMed database; the obtained information was thoroughly analyzed and synthesized. Expert opinion: As cure in advanced RCC cannot be accomplished with the current therapy standards such as tyrosine kinase inhibitors and mammalian target of rapamycin inhibitors, new treatment strategies are being sought. Enhancing the immune system represents an appealing avenue for kidney cancer therapy. Disappointingly, high-dose interleukin-2 and interferon-alpha cause severe toxicity and produce a questionable clinical benefit. The authors postulate that
the ‘durable responses’ seen with these agents in only a handful of RCC patients represent spontaneous remissions. Promising immune strategies in RCC such as anti-cytotoxic T-lymphocyte-associated protein antibodies, anti-programmed cell death 1 (PD1)/PD1 ligand and tumor vaccines may expand the existing options for kidney cancer in future years.

[955]
TÍTULO / TITLE: - Role of choline PET/CT in guiding target volume delineation for irradiation of prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Schwarzenbock SM; Kurth J; Gocke C; Kuhnt T; Hildebrandt G; Krause BJ
INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, University Medical Centre Rostock, Rostock, Germany.
RESUMEN / SUMMARY: - Choline PET/CT has shown limitations for the detection of primary prostate cancer and nodal metastatic disease, mainly due to limited sensitivity and specificity. Conversely in the restaging of prostate cancer recurrence, choline PET/CT is a promising imaging modality for the detection of local regional and nodal recurrence with an impact on therapy management. This review highlights current literature on choline PET/CT for radiation treatment planning in primary and recurrent prostate cancer. Due to limited sensitivity and specificity in differentiating between benign and malignant prostatic tissues in primary prostate cancer, there is little enthusiasm for target volume delineation based on choline PET/CT. Irradiation planning for the treatment of single lymph node metastases on the basis of choline PET/CT is controversial due to its limited lesion-based sensitivity in primary nodal staging. In high-risk prostate cancer, choline PET/CT might diagnose lymph node metastases, which potentially can be included in the conventional irradiation field. Prior to radiation treatment of recurrent prostate cancer, choline PET/CT may prove useful for patient stratification by excluding distant disease which would require systemic therapy. In patients with local recurrence, choline PET/CT can be used to delineate local sites of recurrence within the prostatic resection bed allowing a boost to PET-positive sites. In patients with lymph node metastases outside the prostatic fossa and regional metastatic lymph nodes, choline PET/CT might influence radiation treatment planning by enabling extension of the target volume to lymphatic drainage sites with or without a boost to PET-positive lymph nodes. Further clinical randomized trials are required to assess treatment outcomes following choline-based biological
radiation treatment planning in comparison with conventional radiation treatment planning.

[956]
**TÍTULO / TITLE:** Cutaneous clues to renal cell carcinoma: hereditary leiomyomatosis and renal cell carcinoma.

**RESUMEN / SUMMARY:** We present a case of a 33-year-old female who was incidentally found to have cutaneous leiomyomata during a routine skin examination. Further history revealed that she also suffered from uterine fibroids and that her mother had died at an early age from renal cell carcinoma. This case serves as a reminder of the often-subtle cutaneous clues, as well as the importance of a multidisciplinary approach, for early diagnosis of potentially fatal conditions.


**AUTORES / AUTHORS:** Michelon MA; Layton CJ; Jessup CJ; Lizzul PF

[957]
**TÍTULO / TITLE:** Renal epithelioid angiomyolipoma.

**RESUMEN / SUMMARY:**


**AUTORES / AUTHORS:** Cherif M; Ktari K; Kerkeni W; Bouzouita A; Kourda N; Rajhi H; Ben Slama R; Chebil M

[958]
**TÍTULO / TITLE:** Note on “Simulation optimization of PSA-threshold based prostate cancer screening policies”

**RESUMEN / SUMMARY:**

**REVISTA / JOURNAL:** Health Care Manag Sci. 2013 May 3.

**AUTORES / AUTHORS:** Underwood DJ; Zhang J; Denton BT; Shah ND; Inman BA

**INSTITUCIÓN / INSTITUTION:** Edward P. Fitts Department of Industrial & Systems Engineering, North Carolina State University, Raleigh, NC, 27695, USA, daniel.underwood@ncsu.edu.

[959]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Pal SK; Hsu J; Hsu S; Hu J; Bergerot P; Carmichael C; Saikia J; Liu X; Lau C; Twardowski P; Figlin RA; Yuh BE

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology & Experimental Therapeutics, City of Hope Comprehensive Cancer Center, Duarte, CA.

RESUMEN / SUMMARY: - Clinical outcomes in older adults with metastatic renal cell carcinoma (mRCC) are poorly understood, particularly in the era of targeted therapies. We characterize survival and relevant treatment-related variables in a modern series. From an institutional database including 562 patients with RCC, a total of 219 patients with metastatic disease were identified for the current analysis. Survival was assessed in four age-based cohorts: (1) age < 55, (2) age 55-64, (3) age 65-74, and (4) age >/= 75. The number of lines of therapy rendered was collected for each patient, and the reason for treatment discontinuation was characterized. Of the 219 patients assessed, median age was 58 (range, 26-87), and most patients had clear cell histology (82%) and prior nephrectomy (70.9%). The majority of patients were characterized as intermediate-risk (53%) by MSKCC criteria. Median survival in patients age >/= 75 was 12.5 months, as compared to 26.4 months for patients age < 75 (P=0.003). Patients age >/= 75 received fewer lines of systemic therapy as compared to other age-based subsets, and more frequently discontinued therapies due to toxicity. Older adults represent a unique subpopulation of patients with mRCC, with distinct clinical outcomes. Further research is warranted to better understand the safety and tolerability of current therapies for mRCC in this group.

[960]

TÍTULO / TITLE: - Editorial Comment to Circumcision related to urinary tract infections, sexually transmitted infections, human immunodeficiency virus infections, and penile and cervical cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Shimada K

INSTITUCIÓN / INSTITUTION: - Department of Urology, Osaka Medical Center and Research Institute for Maternal and Child Health, Izumi, Osaka, Japan. shimada@mch.pref.osaka.jp

[961]
Circumcision related to urinary tract infections, sexually transmitted infections, human immunodeficiency virus infections, and penile and cervical cancer.

Male circumcision has been carried out as a prophylactic measure against future diseases, as well as a rite of passage due to religious practice and definite medical indication. The present review discusses the benefits of male circumcision on the prevention of urinary tract infections, and the importance of circumcision in congenital urinary system anomalies, such as vesicoureteral reflux. Additionally, the present review examines the associations between circumcision and sexually transmitted infections, including human immunodeficiency virus, and the preventive effect of circumcision on penile cancer and cervical cancer of female partners.

Selenium and prostate cancer prevention: insights from the selenium and vitamin E cancer prevention trial (SELECT).

The Selenium and Vitamin E Cancer Prevention Trial (SELECT) was conducted to assess the efficacy of selenium and vitamin E alone, and in combination, on the incidence of prostate cancer. This randomized, double-blind, placebo-controlled, 2 x 2 factorial design clinical trial found that neither selenium nor vitamin E reduced the incidence of prostate cancer after seven years and that vitamin E was associated with a 17% increased risk of prostate cancer compared to placebo. The null result was surprising given the strong preclinical and clinical evidence suggesting chemopreventive activity of selenium. Potential explanations for the null findings include the agent formulation and dose, the characteristics of the cohort, and the study design. It is likely that only specific subpopulations may benefit from selenium supplementation; therefore, future studies should consider...
baseline selenium status of the participants, age of the cohort, and genotype of specific selenoproteins, among other characteristics, in order to determine the activity of selenium in cancer prevention.

[963]
**TÍTULO / TITLE:** - Serum Levels of CA15-3, AFP, CA19-9 and CEA Tumor Markers in Cancer Care and Treatment of Patients with Impaired Renal Function on Hemodialysis.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Estakhri R; Ghahramanzade A; Vahedi A; Nourazarian A

**INSTITUCIÓN / INSTITUTION:** - Liver and Gastrointestinal Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran E-mail: estakhri@tbzmed.ac.ir.

**RESUMEN / SUMMARY:** - Since renal failure causes decrease in tumor marker excretion, use of these markers in cancer care and treatment in patients with renal insufficiency or hemodialysis is controversial. The aim of this study was to investigate differences of serum levels of tumor markers CA15-3, AFP, CA19-9 and CEA in patients with impaired renal function. A total of 100 patients referred to the Tabriz Immam Reza and Amiralmomenin hospital from June 2010 to November 2011 were selected for study. Subjects were divided to 3 groups of healthy, dialysis and renal failure but non hemodialysis cases, the last category being re-grouped based on creatinine clearance. No significant relationship between different groups in serum levels of CEA (P=0.99) and CA19-9 (P=0.29) tumor markers was found. A significant correlation was observed between serum levels of AFP (P<0.001) and CA15-3 (P<0.001) and also a tendency between creatinine clearance and CEA (r=0.05, P=0.625). Creatinine clearance significantly correlated with AFP (P<0.001, r=0.53) and CA15-3 (p=0.00, r=-0.412), but not CA19-9 (P=0.089, r=-0.171). According to results of this study it appears that use of tumor markers in patients with impaired renal function should be performed with special precautions.

[964]
**TÍTULO / TITLE:** - Impact of non-dialysis chronic kidney disease on survival in patients with septic shock.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Maizel J; Deransy R; Dehedin B; Secq E; Zogheib E; Lewandowski E; Tribouilloy C; Massy ZA; Choukroun G; Slama M
BACKGROUND: Chronic kidney disease (CKD) is known to expose the patient to a high risk of death due to cardiovascular and infective causes. In parallel, septic shock is a major challenge for cardiovascular and immune system. Therefore, we tried to determine whether non-dialysis CKD, defined as a baseline estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m², for three months prior to the onset of septic shock is an independent risk factor for death.

METHODS: All patients treated in a teaching hospital medical ICU for septic shock between January 2007 and December 2009 were retrospectively analyzed. Patients in whom baseline eGFR could not be determined (n=14) or patients treated by chronic dialysis (n=21) or kidney transplantation (n=14) were excluded. A total of 163 patients were included. The population was divided according to baseline eGFR ≥ 60 ml/min/1.73 m² (non-CKD group, n=107) and < 60 ml/min/1.73 m² (CKD group, n=56). Twenty-eight-day and 1-year survival curves were plotted. Prognostic factors were determined using Cox proportional hazards models.

RESULTS: Baseline eGFR was significantly higher in the non-CKD group than in the CKD group (81 (67-108) vs. 36 (28-44) ml/min/1.73 m², respectively; p=0.001). Age, SAPS II, serum creatinine on admission and the number of patients with a history of diabetes, hypertension, heart failure, peripheral artery disease, coronary artery disease and statin medication were significantly higher in the CKD group than in the non-CKD group. The mortality rate was lower in the non-CKD group than in the CKD group after 28 days (50% vs. 70%, respectively; p=0.03) and 1 year (64% vs. 82%, respectively; p=0.03). On multivariate analysis, the dichotomous variable CKD (eGFR < 60 ml/min/1.73 m²) remained significantly associated with the 28-day and 1-year mortality.

CONCLUSIONS: Non-dialysis CKD appears to be an independent risk factor for death after septic shock.

[965]
TÍTULO / TITLE: Effects of oncological treatments on semen quality in patients with testicular neoplasia or lymphoproliferative disorders.
RESUMEN / SUMMARY: Pretherapy sperm cryopreservation in young men is currently included in good clinical practice guidelines for cancer patients. The aim of this paper is to outline the effects of different oncological treatments on semen quality in patients with testicular neoplasia or lymphoproliferative disorders.

AUTORES / AUTHORS: Di Bisceglie C; Bertagna A; Composto ER; Lanfranco F; Baldi M; Motta G; Barberis AM; Napolitano E; Castellano E; Manieri C
RESUMEN / SUMMARY: Pretherapy sperm cryopreservation in young men is currently included in good clinical practice guidelines for cancer patients. The aim of this paper is to outline the effects of different oncological treatments on semen quality in patients with testicular neoplasia or lymphoproliferative disorders.
disorders, based on an 8-year experience of the Cryopreservation Centre of a large public hospital. Two hundred and sixty-one patients with testicular neoplasia and 219 patients with lymphoproliferative disorders who underwent chemotherapy and/or radiotherapy and pretherapy semen cryopreservation were evaluated. Sperm and hormonal parameters (follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, inhibin B levels) were assessed prior to and 6, 12, 18, 24 and 36 months after the end of cancer treatment. At the time of sperm collection, baseline FSH level and sperm concentration were impaired to a greater extent in patients with malignant testicular neoplasias than in patients with lymphoproliferative disorders. Toxic effects on spermatogenesis were still evident at 6 and 12 months after the end of cancer therapies, while an improvement of seminal parameters was observed after 18 months. In conclusion, an overall increase in sperm concentration was recorded about 18 months after the end of cancer treatments in the majority of patients, even if it was not possible to predict the evolution of each single case ‘a priori’. For this reason, pretherapy semen cryopreservation should be considered in all young cancer patients.

[966]

TÍTULO / TITLE: - Clinical outcomes in patients with stage I non-seminomatous germ cell cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Lv ZJ; Wu S; Dong P; Yao K; He YY; Gui YT; Zhou FJ; Liu ZW; Cai ZM
INSTITUCIÓN / INSTITUTION: - [1] Shenzhen Second People’s Hospital, the First Affiliated Hospital of Shenzhen University, Shenzhen 518036, China [2] Anhui Medical University, Hefei 230032, China.
RESUMEN / SUMMARY: - This study assesses the long-term outcomes in Han Chinese patients with clinical stage I non-seminomatous germ cell testicular cancer (CSI NSGCT) treated with surveillance, retroperitoneal lymph node dissection (RPLND) and adjuvant chemotherapy. We retrospectively evaluated 89 patients with a mean age of 26.5 years. After orchiectomy, 37 patients were treated with surveillance, 34 underwent RPLND and 18 were managed with chemotherapy. The overall survival rate, the recurrence-free survival rate and the risk factors were evaluated. The median follow-up length was 92 months (range: 6-149 months). Thirteen of the 89 patients (14.6%) had relapses, and one died by the evaluation date. The overall survival rate was 98.9%. The cumulative 4-year recurrence-free rates were 80.2%, 92.0% and 100% for the surveillance, RPLND and chemotherapy groups, respectively. The disease-free period tended to be briefer in patients with a history of cryptorchidism and those
with stage Ia. Therefore, surveillance, RPLND and adjuvant chemotherapy might be reliable strategies in compliant patients with CSI NSGCT. Surveillance should be recommended for patients with the lowest recurrence rate, especially those without lymphovascular invasion. This study might aid the establishment of a standard therapy for CSI NSGCT in China. Asian Journal of Andrology advance online publication, 20 May 2013; doi: 10.1038/aja.2013.16.

[967]
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Fujimura T
INSTITUCIÓN / INSTITUTION: Department of Urology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan. fujimurat-uro@h.u-tokyo.ac.jp.

[968]
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Ito H; Sano F; Ogawa T; Yao M
INSTITUCIÓN / INSTITUTION: Department of Urology, Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, Japan.
RESUMEN / SUMMARY: We investigated the Core Lower Urinary Tract Symptom Score as an outcome assessment tool for the treatment of lower urinary tract symptoms using silodosin. In addition, the ability of the Core Lower Urinary Tract Symptom Score to detect overactive bladder in male patients with lower urinary tract symptoms was examined. The present study included 241 males with benign prostatic hyperplasia treated at 31 medical facilities between June 2009 and December 2010. All patients were given silodosin, and the effects of silodosin intake were measured using four questionnaires: the Core Lower Urinary Tract Symptom Score, International Prostate Symptom Score, Overactive Bladder Symptom Score and Quality-of-Life index. The efficacy of silodosin for treating lower urinary tract symptoms was validated according to
the total scores of all four questionnaires weighted equally (P < 0.05). Spearman’s rho among the Core Lower Urinary Tract Symptom Score, International Prostate Symptom Score and Overactive Bladder Symptom Score showed a mild-high correlation. However, the correlation between the baseline values of the Core Lower Urinary Tract Symptom Score and Quality-of-Life index was low in the groups with benign prostatic hyperplasia (rho = 0.314) and benign prostatic hyperplasia/overactive bladder (rho = 0.244). Our findings showed the Core Lower Urinary Tract Symptom Score, both its total score and each subscore, is able to show the efficacy of silodosin, similar to other questionnaires. The Core Lower Urinary Tract Symptom Score is also useful for identifying overactive bladder symptoms in patients with benign prostatic hyperplasia. As the Core Lower Urinary Tract Symptom Score does not correlate well with the Quality-of-Life index, these two questionnaires might be better used in combination to assess treatment outcomes.

[969]
TÍTULO / TITLE: - MRI-based sector analysis enhances prostate palladium-103 brachytherapy quality assurance in a phase II prospective trial of men with intermediate-risk localized prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Takiar V; Pugh TJ; Swanson D; Kudchadker RJ; Bruno TL; McAvoy S; Mahmood U; Frank SJ
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.
RESUMEN / SUMMARY: - PURPOSE: Palladium-103 (103Pd) may be superior to other isotopes in brachytherapy for localized intermediate-risk prostate cancer because of its relatively short half-life, higher initial dose rate, and greater dose heterogeneity within the target volume; these properties also underscore the need for accurate target delineation and postimplant quality assurance. We assessed the use of prostate sector analysis based on MRI for quality assurance after 103Pd monotherapy. METHODS AND MATERIALS: Fifty men with intermediate-risk prostate cancer underwent 103Pd monotherapy in a prospective phase II trial at MD Anderson Cancer Center. Dosimetric analyses on day 30 after the implant were done using both CT and fused CT/MRI scans. Dosimetric variables were assessed for the entire prostate and for each of three or six sectors. Volumes and dosimetric variables were compared with paired t tests. RESULTS: Postimplant dosimetric variables for the entire prostate were significantly different on CT vs. CT/MRI (p = 0.019 for V100 and p
< 0.01 for D90). Prostate volumes were smaller on the CT/MRI scans (p < 0.00001). The base sector contributed the greatest difference, with doses based on CT/MRI lower than those based on CT (p < 0.01 for V100 and D90). To date, these lower base doses have not affected biochemical outcomes for patients with disease in prostate base biopsy samples. CONCLUSIONS: CT/MRI is more precise than CT for prostate volume delineation and dosimetric quality assessment and thus provides superior heterogeneity control assessment after 103Pd monotherapy implants.

[970]
**TÍTULO / TITLE:** Prognostic and Predictive Value of Hematologic Parameters in Patients with Metastatic Renal Cell Carcinoma: Second Line Sunitinib Treatment Following IFN-alpha.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Dirican A; Kucukzeybek Y; Erten C; Somali I; Demir L; Can A; Payzin KB; Bayoglu IV; Akyol M; Yildiz Y; Koeseoglu M; Alacacioglu A; Tarhan MO

**INSTITUCIÓN / INSTITUTION:** Department of Medical Oncology, Izmir Katip Celebi University Ataturk Training and Research Hospital, Tarhan, Turkey E-mail: ahmetdirican@yahoo.com.

**RESUMEN / SUMMARY:** Background: Long-term survival is a problem with locally advanced and metastatic renal cell carcinomas. Sunitinib malate is an oral multitargeted tyrosine kinase inhibitor, but data on sunitinib use as a second line treatment in metastatic renal cell carcinoma (mRCC) are limited. Prognostic and predictive value of peripheral blood markers has been shown for many cancers. Materials and Methods: Efficacy and safety profiles of sunitinib after interferon alpha were evaluated based on retrospective data for 23 patients with mRCC. Hematological parameters (neutrophils, lymphocytes, platelets, mean platelet volume, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio) were recorded at the time of metastasis. It was evaluated whether hematological parameters were prognostic and predictive factors. Results: Median progression-free survival (PFS) time was 16.5 months (95%CI: 0-34.5). Median overall survival (OS) time was 25.7 months (95%CI: 10.8-40.0). Most common side effects were neutropenia (52.2%), stomatitis (26.1%) and hand-food syndrome (26.1%). PFS was found 3.13 vs 17.1 months in patients with neutrophil/lymphocyte ratio (NLR)>3 vs NLR</=3 (p:0.012). Median OS was 6.96 vs 27.1 months in patients with NLR>3 vs NLR</=3 (p:0.001). While 75% of patients who responded to sunitinib had NLR</=3, in 72% of patients with no response to sunitinib NLR>3 was detected (p:0.036). The association between the Memorial Sloan-Kettering Cancer Center (MSKCC) criteria and NLR was statistically significant (p:0.022). Conclusions: Data on second line sunitinib treatment following cytokine in mRCC are limited. In our study, we observed
second line sunitinib treatment following IFN-alpha to be effective and tolerable. NLR appeared to have prognostic and predictive value.

[971]

TÍTULO / TITLE: - Editorial Comment from Dr Hennenberg to Cyclic guanosine monophosphate-enhancing reduces androgenic extracellular regulated protein kinases-phosphorylation/Rho kinase II-activation in benign prostate hyperplasia.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hennenberg M
INSTITUCIÓN / INSTITUTION: - Department of Urology, University of Munich, Munich, Germany. martin.hennenberg@med.uni-muenchen.de.

[972]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Liu CM; Fan YC; Lo YC; Wu BN; Yeh JL; Chen IJ
INSTITUCIÓN / INSTITUTION: - Graduate Institute of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan; Department of Pharmacology, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.
RESUMEN / SUMMARY: - OBJECTIVES: To investigate whether 7-[2-[4-(2-chlorophenyl) piperazinyl] ethyl]-1,3-di-methylxanthine (KMUP-1) inhibits the effects of testosterone on the development of benign prostatic hyperplasia and sensitizes prostate contraction. METHODS: A benign prostatic hyperplasia animal model was established by subcutaneous injections of testosterone (3 mg/kg/day, s.c.) for 4 weeks in adult male Sprague-Dawley rats. Animals were divided into six groups: control, testosterone, testosterone with KMUP-1 (2.5, 5 mg/kg/day), sildenafil (5 mg/kg/day) or doxazosin (5 mg/kg/day). After 4 weeks, the animals were killed, and prostate tissues were prepared for isometric tension measurement and western blotting analysis. KMUP-1, Y27632, zaprinast, doxazosin or tamsulosin were used at various concentrations to determine the contractility sensitized by phenylephrine (10 mumol/L). RESULTS: KMUP-1 inhibited testosterone-induced phosphorylation of extracellular signal-regulated phosphorylated protein kinase and mitogen-activated protein kinase kinase and Rho kinase-II activation. Sildenafil and doxazosin significantly decreased benign prostatic hyperplasia-induced
mitogen-activated protein kinase kinase and Rho kinase-II activation. The decreased expressions of soluble guanylate cyclase alpha1 was reversed by KMUP-1, doxazosin and sildenafil. Soluble guanylate cyclase beta1 and protein kinase G were increased by KMUP-1, doxazosin, and sildenafil in the testosterone-treated benign prostatic hyperplasia group. Phosphodiesterase-5 was increased by testosterone and inhibited by KMUP-1 (5 mg/kg/day) or sildenafil (5 mg/kg/day). KMUP-1 inhibited phenylephrine-sensitized prostate contraction of rats treated with testosterone. CONCLUSIONS: Mitogen-activated protein kinase 1/extracellular regulated protein kinases kinase, soluble guanylate cyclase/cyclic guanosine monophosphate, protein kinase/protein kinase G and Rho kinase-II are related to prostate smooth muscle tone and proliferation induced by testosterone. KMUP-1 inhibits testosterone-induced prostate hyper-contractility and mitogen-activated protein kinase 1/extracellular regulated protein kinases kinase-phosphorylation, and it inactivates Rho kinase-II by cyclic guanosine monophosphate, protein kinase and alpha1A-adenergic blockade. Thus, KMUP-1 might be a beneficial pharmacotherapy for benign prostatic hyperplasia.
**INSTITUCIÓN / INSTITUTION:** - Division of Radiation Oncology, Department of Oncology, University of Alberta, Cross Cancer Institute, Edmonton, AB.

**RESUMEN / SUMMARY:** - PURPOSE: The objective of the present study was to analyze, with relatively high sensitivity and specificity, uptake properties of [(11)C]-choline in prostate cancer patients by means of positron-emission tomography (PET)/computed tomography (CT) imaging using objectively defined PET parameters to test for statistically significant changes before, during, and after external-beam radiation therapy (EBRT) and to identify the time points at which the changes occur. METHODS: The study enrolled 11 patients with intermediate-risk prostate cancer treated with EBRT, who were followed for up to 12 months after EBRT. The [(11)C]-choline PET scans were performed before treatment (baseline); at weeks 4 and 8 of EBRT; and at 1, 2, 3, 6, and 12 months after EBRT. RESULTS: Analysis of [(11)C]-choline uptake in prostate tissue before treatment resulted in a maximum standardized uptake value (SUVmax) of 4.0 +/- 0.4 (n = 11) at 40 minutes after injection. During week 8 of EBRT, the SUVmax declined to 2.9 +/- 0.1 (n = 10, p < 0.05). At 2 and 12 months after EBRT, SUVmax values were 2.3 +/- 0.3 (n = 10, p < 0.01) and 2.2 +/- 0.2 (n = 11, p < 0.001) respectively, indicating that, after EBRT, maximum radiotracer uptake in the prostate was significantly reduced. Similar effects were observed when analyzing the tumour:muscle ratio (TMR). The TMR declined from 7.4 +/- 0.6 (n = 11) before EBRT to 6.1 +/- 0.4 (n = 11, nonsignificant) during week 8 of EBRT, to 5.6 +/- 0.03 (n = 11, p < 0.05) at 2 months after EBRT, and to 4.4 +/- 0.4 (n = 11, p < 0.001) at 12 months after EBRT. CONCLUSIONS: Our study demonstrated that intraprostatic [(11)C]-choline uptake in the 11 analyzed prostate cancer patients significantly declined during and after EBRT. The PET parameters SUVmax and TMR also declined significantly. These effects can be detected during radiation therapy and up to 1 year after therapy. The prognostic value of these early and statistically significant changes in intraprostatic [(11)C]-choline PET avidity during and after EBRT are not yet established. Future studies are indicated to correlate changes in [(11)C]-choline uptake parameters with long-term biochemical recurrence to further evaluate [(11)C]-choline PET changes as a possible, but currently unproven, biomarker of response.

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**TÍTULO / TITLE:** - Expression profiling of metastatic renal cell carcinoma using gene set enrichment analysis.

**RESUMEN / SUMMARY:** - **Enlace al Resumen / Link to its Summary**


**AUTORES / AUTHORS:** - Maruschke M; Hakenberg OW; Koczán D; Zimmermann W; Stief CG; Buchner A

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, University of Rostock, Rostock.
RESUMEN / SUMMARY: - OBJECTIVE: To identify complex changes in cell biology occurring during metastatic progression of renal cell carcinoma using a novel gene expression analysis algorithm. METHODS: Whole genome expression profiling was carried out on 32 snap-frozen samples of clear-cell renal cell carcinoma metastases, 29 primary tumors (14 low grade, 15 high grade) and 14 samples of normal kidney tissue using oligonucleotide microarrays. These data were analyzed with the gene set enrichment analysis method, which is able to detect even small, but significant, expression changes in functionally connected genes that cannot be shown by gene-by-gene comparisons. RESULTS: There were 95 gene sets (pathways) with significant upregulation in metastases compared with normal kidney tissue (P < 0.01), and 77 gene sets with significant downregulation, respectively. Low-grade and high-grade tumors showed deregulation of various pathways that have previously not been described in renal cell carcinoma. There were significant changes of genes involved in cell cycle control, apoptosis, cell motility, metabolism, cell adhesion and cytoskeleton. Some promising new potential therapy targets were identified in renal cell carcinoma metastases; for example, aurora-kinase A and flap structure-specific endonuclease 1. CONCLUSION: Expression profiling of metastatic renal cell carcinoma using the gene set enrichment analysis pathway analysis method provides new and detailed insights in alterations occurring in renal cell carcinoma during malignant transformation and progression. These data can help to develop new and specifically targeted renal cell carcinoma therapies.

[976]
TÍTULO / TITLE: - Letter to the editor: is routine screening necessary for renal cell carcinoma in end-stage renal disease patients?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 4111/kju.2013.54.4.277
AUTORES / AUTHORS: - Ghadian A
INSTITUCIÓN / INSTITUTION: - Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.

[977]
TÍTULO / TITLE: - Editorial Comment to Predictors of benign histology in clinical T1a renal cell carcinoma tumors undergoing partial nephrectomy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1111/iju.12191
AUTORES / AUTHORS: - Izumi K

716
Predictors of benign histology in clinical T1a renal cell carcinoma tumors undergoing partial nephrectomy.

Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 1111/iju.12166

AUTORES / AUTHORS: Fujita T; Iwamura M; Wakatabe Y; Nishi M; Ishii D; Matsumoto K; Yoshida K; Baba S

La anatomía de las características de los tumores renales ha sido clasificada utilizando varios sistemas. Se prevé una asociación entre las características anatomáticas de los tumores y su diagnóstico postoperatorio histológico. La presente investigación se realizó con el objetivo de evaluar el porcentaje de diagnósticos benignos en tumores renales que fueron diagnosticados como T1a antes de la cirugía. Desde enero de 2000 hasta diciembre de 2010, 149 pacientes fueron sometidos a nefrectomía parcial (abierta o laparoscópica) para T1a cáncer de célula renal. La frecuencia de hallazgos histológicos benignos se evaluó. El análisis de regresión logística estimó la importancia relativa de los factores predictivos. La frecuencia global de lesiones benignas fue 8.1%. El análisis multivariado identificó tres factores predictivos significativamente estadísticamente significativos para las lesiones benignas: edad, sexo y propiedad exófitica del tumor (P = 0.0356, 0.0183 y 0.0330, respectivamente). Los hallazgos actuales sugieren que los tumores exófiticos con características anteriores pueden ser más propensos a ser benignos en la histología después de la nefrectomía parcial.

Protein Expression of ZEB2 in Renal Cell Carcinoma and Its Prognostic Significance in Patient Survival.

Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0062558

AUTORES / AUTHORS: Fang Y; Wei J; Cao J; Zhao H; Liao B; Qiu S; Wang D; Luo J; Chen W
INSTITUCIÓN / INSTITUTION: Department of Urology, First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China.

RESUMEN / SUMMARY: BACKGROUND: ZEB2 has been reportedly shown to mediate the epithelial-to-mesenchymal transition (EMT) and disease aggressiveness in human tumors. However, the expression status of ZEB2 in renal cell carcinoma (RCC) and ZEB2’s clinicopathologic/prognostic significance are poorly understood. METHODOLOGY PRINCIPAL FINDINGS: In this study, tissue microarray, immunohistochemistry (IHC) and western blot analyses were utilized to investigate the ZEB2 expression status in RCC and adjacent renal tissue samples. In our study, samples from 116 RCC patients treated with radical nephrectomy were used as a training set to generate a ZEB2 optimal cut-point for patient outcome by receiver operating characteristic (ROC) analysis. For validation, the correlation of ZEB2 expression with the clinical characteristics and patient outcomes in another set (including 113 patients) was analyzed to validate the obtained cut-point. In the training and validation sets, high expression of ZEB2, defined by ROC analysis, predicted a poorer overall survival and progression-free survival, as evidenced by the univariate and multivariate analyses. In different subsets of overall patients, ZEB2 expression was also a prognostic indicator in patients with stage I/II, stage III/IV, grade ½ and grade ¾ disease (P<0.05). Downregulation of ZEB2 by shRNA decreased the migration and invasion ability of 769-P cells in vitro. Furthermore, high ZEB2 expression was positively correlated with vimentin expression and inversely linked to E-cadherin expression in RCC. CONCLUSION SIGNIFICANCE: Our findings provide a basis for the concept that high ZEB2 expression in RCC may be important in the acquisition of an aggressive phenotype. This evidence suggests that ZEB2 overexpression (examined by IHC) is an independent biomarker for the poor prognosis of patients with RCC.

[980]

CASTELLANO:


TÍTULO / TITLE: Interstitial hyperthermia of the prostate in combination with brachytherapy : An evaluation of feasibility and early tolerance.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Kukielka AM; Hetnal M; Brandys P; Walasek T; Dabrowski T; Pluta E; Nahajowski D; Kudzia R
INSTITUCIÓN / INSTITUTION: - Department of Radiotherapy, Centre of Oncology, M. Sklodowska Curie Institute, Krakow Branch, ul. Garncarska 11, 31-115, Krakow, Poland, drkukielka@gmail.com.

RESUMEN / SUMMARY: - OBJECTIVE: A retrospective study to evaluate the feasibility and toxicity of interstitial hyperthermia (IHT) combined with high-dose-rate (HDR) brachytherapy as the initial treatment for low- and intermediate-risk prostate cancer, and as a salvage therapy in previously irradiated patients with local recurrence. PATIENTS AND METHODS: Between 18 December 2008 and 5 September 2012, 73 prostate cancer patients were treated with interstitial HDR brachytherapy of the prostate combined with IHT. In 54 patients this was the initial therapy for prostate cancer, while the other 19 were treated for local recurrence after previously undergoing external beam radiotherapy (EBRT). Toxicity for the organs of the genitourinary system and rectum was assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) v. 4.03 within 3 months after treatment. RESULTS: Median follow-up was 15 months (range 3-46). The combination of HDR brachytherapy and IHT was well tolerated. The toxicity profile was similar to that of HDR brachytherapy when not combined with hyperthermia. The most common minor complications were urinary frequency (grade 1: 37 %; grade 2: 22 %), nocturia (three times per night: 29 %; four- or more times per night: 20 %) and transient weakening of the urine stream (grade 1: 36 %; grade 2: 11 %). No early rectal complications were observed in the patient group and the severity of genitourinary toxicity was only grade 1-2. CONCLUSION: Early tolerance of IHT in combination with HDR brachytherapy is good. Further prospective clinical studies should focus on the effects of combining IHT with HDR brachytherapy and the influence of this adjuvant therapy on biochemical disease-free survival, local control and overall survival.

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[TÍTULO / TITLE: - Sentinel lymph node dissection in more than 1200 prostate cancer cases: Rate and prediction of lymph node involvement depending on preoperative tumor characteristics.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Winter A; Kneib T; Henke RP; Wawroschek F

INSTITUCIÓN / INSTITUTION: - Department of Urology and Pediatric Urology, Clinical Center Oldenburg, European Medical School Oldenburg-Groningen, Oldenburg.

RESUMEN / SUMMARY: - OBJECTIVES: To stratify the rate and prediction of lymph node involvement in prostate cancer patients undergoing sentinel-lymphadenectomy depending on preoperative tumor characteristics, and to
compare the outcome with the European Association of Urology Guideline indication for lymphadenectomy. METHODS: A total of 1229 patients (median age 66 years) were treated with open sentinel-lymphadenectomy and prostatectomy between 2005 and 2009. Median preoperative prostate-specific antigen was 7.4 ng/mL. The rate of lymph node involvement was analyzed for D'Amico risk groups. Multivariable logistic regression was used to estimate the probability of lymph node involvement. Predictor variables included preoperative prostate-specific antigen, clinical T-category and biopsy Gleason sum. Predictive accuracy has been quantified (area under the curve) and lymph node positive patients were verified under consideration of the recommended European threshold for lymphadenectomy (nomogram-predicted lymph node invasion risk of >7%). RESULTS: The median number of lymph nodes removed was 10 (interquartile range 7-13). Overall, 17.1% of patients had lymph node involvement; 3.2% in low-, 14.8% in intermediate- and 37.4% in high-risk disease. The predicted risk for lymph node involvement ranged from 2% (prostate-specific antigen \( \leq 4 \) ng/mL, T1, Gleason sum \( \leq 6 \)) to 87% (prostate-specific antigen \( >20 \) ng/mL, T3, Gleason sum \( \geq 8 \)). The predictive accuracy was 82.1%. According to the European guidelines, 15.9% of all lymph node involved cases would not have been detected. CONCLUSIONS: The rate of lymph node involvement seems to be higher in the examined sentinel collective than expected according to the European Guideline nomogram. The first sentinel-based lymph node involvement prediction model can assist in deciding on the indication for sentinel-lymphadenectomy. The validation of a corresponding sentinel-based nomogram is still missing.

[982]

TÍTULO / TITLE: - Anxiety Status and its Relationship with General Health Related Quality of Life among Prostate Cancer Patients in Two University Hospitals in Kuala Lumpur, Malaysia.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Isa MR; Moy FM; Abdul Razack AH; Md Zainuddin Z; Zainal NZ

INSTITUCIÓN / INSTITUTION: - Population Health & Preventive Medicine, Faculty of Medicine, Universiti Teknologi Mara (UiTM) Sungai Buloh Campus, Jalan Hospital, Selangor Darul Ehsan, Malaysia; Julius Centre, Dept. of Social & Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia.

RESUMEN / SUMMARY: - BACKGROUND: This study aimed to determine the prevalence of anxiety among prostate cancer patients, and to ascertain the association between stress status, socio-demographic, medical and surgical illness, current urinary problem and cancer status with general health-related
quality of life (HRQOL) among these patients. METHODS: A hospital based, cross sectional study was conducted at Surgical Clinic, University Malaya Medical Centre (UMMC) and Universiti Kebangsaan Malaysia Medical Centre (UKMMC) using universal sampling. RESULT: A total of 193 patients were recruited. The prevalence of anxiety was 25.4% (95%CI: 19.2 - 31.6). The anxiety ratings were mild anxiety (10.4%), moderate anxiety (13.6%) and severe anxiety (1.6%). The total quality of life among stress group was 59.2 +/- 14.7 and among non-stress group was 73.9 +/- 12.7. There was a significant negative weak correlation between anxiety score and total quality of life (rs=-0.534, P<0.001). In multivariable analysis, there was a significant difference in the total quality of life (QOL) among anxiety status [adj. mean diff. = -9.1 (95%CI: -15.2, -4.7)]. The adjusted mean difference was associated by age category of the patients (P<0.001); living partner (P<0.001); intermittency (P=0.035) and problem of hematuria during micturition (P=0.005).

CONCLUSION: The prevalence of anxiety among prostate cancer was moderately high. Treating the urination problem as well as encouraging living with spouse/family may improve the quality of life among anxiety condition of these patients.

[983]

TÍTULO / TITLE: - Transcriptional network of androgen receptor in prostate cancer progression.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Takayama KI; Inoue S
INSTITUCIÓN / INSTITUTION: - Department of Anti-Aging Medicine, The University of Tokyo, Tokyo, Japan; Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan.
RESUMEN / SUMMARY: - The androgen receptor belongs to the nuclear receptor superfamily and functions as a ligand-dependent transcription factor. It binds to the androgen responsive element and recruits coregulatory factors to modulate gene transcription. In addition, the androgen receptor interacts with other transcription factors, such as forkhead box A1, and other oncogenic signaling pathway molecules that bind deoxyribonucleic acid and regulate transcription. Androgen receptor signaling plays an important role in the development of prostate cancer. Prostate cancer cells proliferate in an androgen-dependent manner, and androgen receptor blockade is effective in prostate cancer therapy. However, patients often progress to castration-resistant prostate cancer with elevated androgen receptor expression and hypersensitivity to androgen. Recently, comprehensive analysis tools, such as complementary DNA microarray, chromatin immunoprecipitation-on-chip and chromatin
immunoprecipitation-sequence, have described the androgen-mediated diverse transcriptional program and gene networks in prostate cancer. Furthermore, functional and clinical studies have shown that some of the androgen receptor-regulated genes could be prognostic markers and potential therapeutic targets for the treatment of prostate cancer, particularly castration-resistant prostate cancer. Thus, identifying androgen receptor downstream signaling events and investigating the regulation of androgen receptor activity is critical for understanding the mechanism of carcinogenesis and progression to castration-resistant prostate cancer.

[984]


RESUMEN / SUMMARY: Estimation of the prevalence and identification of risk factors associated with chronic kidney disease (CKD) diagnosis and survival in dogs. Purebred dogs were hypothesized to have higher CKD risk and poorer survival characteristics than crossbred dogs. Animals: A merged clinical database of 107,214 dogs attending 89 UK veterinary practices over a 2-year period (January 2010-December 2011). METHODS: A longitudinal study design estimated the apparent prevalence (AP) whereas the true prevalence (TP) was estimated using Bayesian analysis. A nested case-control study design evaluated risk factors. Survival analysis used the Kaplan-Meier survival curve method and multivariable Cox proportional hazards regression modeling. RESULTS: The CKD AP was 0.21% (95% CI: 0.19-0.24%) and TP was 0.37% (95% posterior credibility interval 0.02-1.44%). Significant risk factors included increasing age, being insured, and certain breeds (Cocker Spaniel, Cavalier King Charles Spaniel). Cardiac disease was a significant comorbid disorder. Significant clinical signs included halitosis, weight loss, polyuria/polydipsia, urinary incontinence, vomiting, decreased appetite, lethargy, and diarrhea. The median survival time from diagnosis was 226 days (95% CI 112-326 days). International Renal Interest Society stage and blood urea nitrogen concentration at diagnosis were significantly associated with hazard of death due to CKD.

CONCLUSION AND CLINICAL IMPORTANCE: Chronic kidney disease...
compromises dog welfare. Increased awareness of CKD risk factors and association of blood biochemistry results with survival time should facilitate diagnosis and optimize case management to improve animal survival and welfare.

[985]
**Título / Title:** Bone metastases and bone loss medical treatment in prostate cancer patients.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary


**Autores / Authors:** Safriadi F

**Institución / Institution:** Department of Urology, Faculty of Medicine, Padjajaran University - Hasan Sadikin Hospital. Jl. Pasteur no 38 Bandung, Indonesia. safriadif@yahoo.com

**Resumen / Summary:** Prostate cancer is a malignancy in urology with the highest incidence metastasize to the bone up to 70%. The incidence of skeletal related event (SRE) by 46.1% such as severe pain, pathologic fractures, spinal compression syndrome and hypercalcemia, with a consequence of higher inpatient care and worsen the patient’s prognosis. Androgen deprivation therapy (ADT) as a metastatic prostate cancer treatment itself causes an osteopenia or osteoporosis. Bisphosphonate inhibits normal and pathologic osteoclast-mediated bone resorption by several mechanisms. Denosumab is the latest treatment option in bone metastases. Multi-study shows the efficacy of denosumab is better than zoledronic acid for SRE prevention. Adverse events between denosumab and bisphosphonate are comparable.

[986]
**Título / Title:** Oncological outcomes in patients with stage I testicular seminoma and nonseminoma: pathological risk factors for relapse and feasibility of surveillance after orchiectomy.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary

**Revista / Journal:** Diagn Pathol. 2013 Apr 8;8:57. doi: 10.1186/1746-1596-8-57

**Autores / Authors:** Kobayashi K; Saito T; Kitamura Y; Nobushita T; Kawasaki T; Hara N; Takahashi K

**Institución / Institution:** Department of Urology, Niigata Cancer Center Hospital, Kawagishi-cho 2, Niigata 951-8566, Japan. harasho@med.niigata-u.ac.jp

**Resumen / Summary:** Background: Surveillance after orchiectomy has recently been a management option in patients with stage I seminoma, while it remains controversial in those with stage I nonseminoma, and the risk factor
associated with relapse is still a matter of concern in both entities. This study was performed to explore pathological risk factors for post-orchiectomy relapse in patients with stage I seminoma and nonseminoma, and to assess oncological outcomes in those managed with surveillance. METHODS: In this single institution study, 118 and 40 consecutive patients with stage I seminoma and nonseminoma were reviewed, respectively. Of the 118 patients with stage I seminoma, 56 and one received adjuvant radiotherapy and chemotherapy, respectively, and 61 were managed with surveillance. Of the 40 men with stage I nonseminoma, 4 underwent adjuvant chemotherapy and 36 were managed with surveillance. RESULTS: No patient had cause-specific death during the mean observation period of 104 and 99 months in men with seminoma and nonseminoma, respectively. In men with stage I seminoma, 1 (1.7%) receiving radiotherapy and 4 (6.6%) men managed with surveillance had disease relapse; the 10-year relapse-free survival (RFS) rate was 93.4% in men managed with surveillance, and their RFS was not different from that in patients receiving adjuvant radiotherapy (logrank P=0.15). Patients with tunica albuginea involvement showed a poorer RFS than those without (10-year RFS rate 80.0% vs. 94.1%), although the difference was of borderline significance (P=0.09). In men with stage I nonseminoma, 9 (22.5%) patients experienced relapse. Patients with lymphovascular invasion seemingly had a poorer RFS than those without; 40.0% and 18.7% of the patients with and without lymphovascular invasion had disease relapse, respectively, although the difference was not significant (logrank P=0.17). CONCLUSION: In both men with stage I seminoma and nonseminoma, surveillance after orchiectomy is a feasible option. However, disease extension through tunica albuginea might be a factor associated with disease relapse in patients with organ-confined seminoma, and those with stage I nonseminoma showing lymphovascular invasion may possibly be at high risk for disease relapse.

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[987]
TÍTULO / TITLE: - Editorial Comment to Bladder recurrence after radical nephroureterectomy: Predictors and impact on oncological outcomes.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
••Enlace al texto completo (gratuito o de pago) 1111/iju.12135
AUTORES / AUTHORS: - Milojevic B
INSTITUCIÓN / INSTITUTION: - Clinic of Urology, Clinical Center of Serbia, Belgrade, Serbia. em2bogomir@yahoo.com.

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[988]
TÍTULO / TITLE: - Clinical significance of amyloid precursor protein in patients with testicular germ cell tumor.

724
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1155/2013/348438
AUTORES / AUTHORS: - Yamada Y; Fujimura T; Takahashi S; Takayama K; Urano T; Murata T; Obinata D; Ouchi Y; Homma Y; Inoue S
INSTITUCIÓN / INSTITUTION: - Department of Urology, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan; Department of Urology, National Center of Global Health and Medicine, Shinjuku-ku, Tokyo, Japan.
RESUMEN / SUMMARY: - Introduction. The biological role of amyloid precursor protein (APP) is not well understood, especially in testicular germ cell tumors (TGCTs). Therefore, we aimed to investigate the immunoreactivity (IR) and expression of APP in TGCTs and evaluated its clinical relevance. Materials and Methods. We performed an analysis of immunohistochemistry and mRNA expression of APP in 64 testicular specimens and 21 snap-frozen samples obtained from 1985 to 2004. We then evaluated the association between APP expression and clinicopathological status in TGCTs. Results. Positive APP IR was observed in 9.8% (4/41) of seminomatous germ cell tumors (SGCTs) and 39.1% (9/23) of nonseminomatous germ cell tumors (NGCTs). NGCTs showed significantly more cases of positive IR (P = 0.00870) and a higher mRNA expression level compared with those of SGCTs (P = 0.0140). Positive APP IR was also significantly associated with alpha-fetoprotein (alpha FP) elevation (P = 0.00870) and venous invasion (P = 0.0414). Conclusion. We observed an elevated APP expression in TGCTs, especially in NGCTs. APP may be associated with a more aggressive cancer in TGCTs.

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TÍTULO / TITLE: - Immunohistochemical analysis of the expression of MAGE-A and NY-ESO-1 cancer/testis antigens in diffuse large B-cell testicular lymphoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1186/1479-5876-11-123
AUTORES / AUTHORS: - Hudolin T; Kastelan Z; Ilic I; Levarda-Hudolin K; Basic-Jukic N; Rieken M; Spagnoli GC; Juretic A; Mengus C
INSTITUCIÓN / INSTITUTION: - Department of Urology, Zagreb University Hospital Center, Zagreb, Croatia. tvrtkohudolin@gmail.com.
RESUMEN / SUMMARY: - BACKGROUND: Primary testicular lymphoma (PTL) is a rare and lethal disease. The most common histological subtype is diffuse large B-cell lymphoma (DLBCL). Standard treatments are frequently ineffective. Thus, the development of novel forms of therapy is urgently required. Specific
immunotherapy generating immune responses directed against antigen predominantly expressed by cancer cells such as cancer-testis antigens (CTA) may provide a valid alternative treatment for patients bearing PTL, alone or in combination with current therapies. METHODS: Three monoclonal antibodies (mAbs), 77B recognizing MAGE-A1, 57B recognizing an epitope shared by multiple MAGE-A CTA (multi-MAGE-A specific) and D8.38 recognizing NY-ESO-1/LAGE-1 were used for immunohistochemical staining of 27 PTL, including 24 DLBCL. RESULTS: Expression of MAGE-A1 was infrequently detectable in DLBCL specimens (12.50%), whereas multi-MAGE-A and NY-ESO-1/LAGE-1 specific reagents stained the cytoplasms of tumor cells in DLBCL specimens with higher frequencies (54.17% and 37.50%, respectively) with different expression levels. CONCLUSIONS: These results suggest that MAGE-A and NY-ESO-1/LAGE-1, possibly in combination with other CTA, might be used as targets for specific immunotherapy in DLBCL.

[990]

TÍTULO / TITLE: - Electroacupuncture for moderate and severe benign prostatic hyperplasia: a randomized controlled trial.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wang Y; Liu B; Yu J; Wu J; Wang J; Liu Z
INSTITUCIÓN / INSTITUTION: - Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China.
RESUMEN / SUMMARY: - PURPOSE: To evaluate the effects of electroacupuncture (EA) on the International Prostate Symptom Score (IPSS), postvoid residual urine (PVR), and maximum urinary flow rate (Qmax), and explore the difference between EA at acupoints and non-acupoints in patients with moderate to severe benign prostate hyperplasia (BPH). SUBJECTS AND METHODS: Men with BPH and IPSS >/=8 were enrolled. Participants were randomly allocated to receive EA at acupoint (treatment group, n = 50) and EA at non-acupoint (control group, n = 50). The primary outcome measure includes the change of IPSS at the 6th week and the secondary outcome measures include changes of PVR and Qmax at the 6th week and change of IPSS at the 18th week. RESULTS: 100/192 patients were included. At the 6th week, treatment group patients had a 4.51 (p<0.001) and 4.12 (p<0.001) points greater decline in IPSS than the control group in the intention to treat (ITT) and per-protocol (PP) populations. At the 18th week, a 3.2 points (p = 0.001) greater decline was found in IPSS for the treatment. No significant differences were found between the two groups in Qmax at the 6th week (p = 0.819). No
significant difference was observed in PVR (P = 0.35). CONCLUSION: Acupoint EA at BL 33 had better effects on IPSS, but no difference on PVR and Qmax as compared with non-acupoint EA. The results indicate that EA is effective in improving patient’s quality of life and acupoint may have better therapeutic effects than non-acupoints in acupuncture treatments of BPH. TRIAL REGISTRATION: ClinicalTrials.gov NCT01218243.

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[991] TÍTULO / TITLE: - Update of randomized trials for prostate cancer screening.
RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary]
AUTORES / AUTHORS: - Vellekoop A; Loeb S
INSTITUCIÓN / INSTITUTION: - Department of Urology, New York University, New York, NY.

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RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary]
AUTORES / AUTHORS: - Xu J; Sun J; Zheng SL
INSTITUCIÓN / INSTITUTION: - 1] Fudan Institute of Urology, Huashan Hospital, Fudan UniversityFudan Institute of Urology, Huashan Hospital, Fudan University, Shanghai 200040, China [2] State Key Laboratory of Genetic Engineering, Fudan University, Shanghai 200433, China [3] Center for Genetic Epidemiology, School of Life Sciences, Fudan University, Shanghai 200433, China [4] Center for Cancer Genomics, Wake Forest School of Medicine, Winston-Salem, NC 27157, USA.
RESUMEN / SUMMARY: - Prostate cancer (PCa) is one of the most common cancers among men in Western developed countries and its incidence has increased considerably in many other parts of the world, including China. The etiology of PCa is largely unknown but is thought to be multifactorial, where inherited genetics plays an important role. In this article, we first briefly review results from studies of familial aggregation and genetic susceptibility to PCa. We then recap key findings of rare and high-penetrance PCa susceptibility genes from linkage studies in PCa families. We devote a significant portion of this article to summarizing discoveries of common and low-penetrance PCa risk-associated single-nucleotide polymorphisms (SNPs) from genetic association studies in PCa cases and controls, especially those from genome-wide association studies (GWASs). A strong focus of this article is to review the literature on the potential clinical utility of these implicated genetic markers.
Most of these published studies described PCa risk estimation using a genetic score derived from multiple risk-associated SNPs and its utility in determining the need for prostate biopsy. Finally, we comment on the newly proposed concept of genetic score; the notion is to treat it as a marker for genetic predisposition, similar to family history, rather than a diagnostic marker to discriminate PCa patients from non-cancer patients. Available evidence to date suggests that genetic score is an objective and better measurement of inherited risk of PCa than family history. Another unique feature of this article is the inclusion of genetic association studies of PCa in Chinese and Japanese populations.

[993]

**TÍTULO / TITLE:** - DPP4 genetic variants influence baseline prostate-specific antigen levels: the J-MICC study.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Higashibata T; Naito M; Mori A; Ozawa N; Furuta M; Tsuchiya R; Koyama E; Morita E; Kawai S; Okada R; Yin G; Wakai K; Hamajima N

**INSTITUCIÓN / INSTITUTION:** - Department of Preventive Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan. h-bata@med.nagoya-u.ac.jp

**RESUMEN / SUMMARY:** - Prostate specific antigen (PSA) testing plays a major role in prostate cancer screening; however, the low positive predictive value of PSA testing leads to many unnecessary biopsies. Genetic background is one of factors that could cause it. That’s why an association between genetic background and PSA levels should be elucidated. This study aimed to investigate whether DPP4 genetic variants are associated with baseline PSA levels. A cross-sectional study was performed on 2,074 Japanese men aged between 35 and 69 in the Shizuoka area from the Japan Multi-institutional Collaborative Cohort (J-MICC) Study. Three DPP4 tagging single nucleotide polymorphisms (SNPs) were selected for genotyping: rs3788979 (A/G), rs7608798 (T/C), and rs2268889 (A/G). Higher mean serum PSA levels were significantly associated with an increase in the number of the rs7608798 C allele (p for trend = 0.02). A stratified analysis by age groups demonstrated that PSA levels had positive significant trends with the numbers of the minor alleles of rs3788979 or rs7608798 in the oldest group (men aged between 60 and 69) (p for trend=0.004 for rs3788979 and p for trend=0.001 for rs7608798). Haplotype analysis showed that the C-A (rs7608798-rs2268889) haplotype was significantly associated with increased PSA levels (p=0.006), compared with the most common haplotype, T-A. In summary, our study suggests that DPP4
genetic variants influence baseline PSA levels, especially in men aged between 60 and 69.

[994]
- **TÍTULO / TITLE:** Editorial Comment from Dr Murtola to Reduction of prostate cancer incidence by naftopidil, an alpha1-adrenoceptor antagonist and transforming growth factor-beta signaling inhibitor.
- **RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1111/iju.12175
- **AUTORES / AUTHORS:** Murtola TJ
- **INSTITUCIÓN / INSTITUTION:** Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA.
  teemu.murtola@uta.fi.

[995]
- **TÍTULO / TITLE:** Editorial Comment from Dr Chen to Reduction of prostate cancer incidence by naftopidil, an alpha1-adrenoceptor antagonist and transforming growth factor-beta signaling inhibitor.
- **RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1111/iju.12174
- **AUTORES / AUTHORS:** Chen IJ
- **INSTITUCIÓN / INSTITUTION:** Department of Pharmacology, Kaohsiung Medical University, Kaohsiung, Taiwan. ingjun@kmu.edu.tw.

[996]
- **TÍTULO / TITLE:** Reduction of prostate cancer incidence by naftopidil, an alpha-adrenoceptor antagonist and transforming growth factor-beta signaling inhibitor.
- **RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1111/iju.12156
- **AUTORES / AUTHORS:** Yamada D; Nishimatsu H; Kumano S; Hirano Y; Suzuki M; Fujimura T; Fukuharu H; Enomoto Y; Kume H; Homma Y
- **INSTITUCIÓN / INSTITUTION:** Department of Urology, The University of Tokyo Hospital; Department of Urology, The Fraternity Memorial Hospital, Tokyo, Japan.
- **RESUMEN / SUMMARY:** OBJECTIVES: Quinazoline-based alpha1-adrenoceptor antagonists are known to inhibit prostate tumor growth through induction of apoptosis. We investigated the effect of a naphthalene-based
alpha1-adrenoceptor antagonist, naftopidil, on prostate cancer incidence, apoptosis of prostatic cell and transforming growth factor-beta signaling. METHODS: Prescription records were linked to pathological data for men who continued naftopidil (n = 766) or tamsulosin (n = 1015) for 3 months or longer between 2003 and 2010. Prostate cancer incidence was analyzed by log-rank test and the Cox proportional hazards model. Apoptosis and cell cycle arrest in human tissues were assessed by immunohistochemical detection of Bcl2 and p21, respectively. Growth inhibition and apoptosis treatment with naftopidil and tamsulosin were assessed in cancer cell lines. Interference with transforming growth factor-beta signaling was examined by western blot analysis. RESULTS: Prostate cancer incidence was significantly lower in men who received naftopidil for 3 months or longer compared with tamsulosin (P = 0.035). Multivariate analysis confirmed a decreased hazard ratio, 0.46, for naftopidil use (P = 0.013), which was more evident with longer treatment. Immunohistochemical positivity for Bcl2, a marker for resistance to apoptosis, was less frequently detected in prostate cancer cells of men who received naftopidil compared with tamsulosin (P < 0.05). Naftopidil inhibited cancer cell growth, induced apoptosis and blocked Smad2 phosphorylation activated by transforming growth factor-beta in cell lines, with a half maximal inhibitory concentration of 1.1 micromol/L. CONCLUSIONS: Naftopidil seems to reduce prostate cancer incidence, possibly by inducing apoptosis, preferentially in cancer cells, and blocking transforming growth factor-beta signaling.
(SEER) Registry was used to identify patients aged 18 and older diagnosed stage IV RCC between 1992 and 2009. Patients had documented clear cell, papillary or chromophobe histology. The Kaplan Meier method and log-rank test were used to compare disease-specific survival (DSS) for patients diagnosed from 1992-2004 (i.e., the cytokine era) and 2005-2009 (i.e., the targeted therapy era). Univariate and multivariate analyses of relevant clinicopathologic characteristics were also performed. RESULTS: Of 5,176 patients identified using the above characteristics, 2,392 patients were diagnosed from 1992-2004 and 2,784 from 2005-2009. Median DSS was improved in those patients diagnosed from 2005-2009 (16 months vs 13 months; P<0.001). A similar temporal trend towards improving survival was noted in patients with clear cell (P = 0.0006), but not in patients with non-clear cell disease (P = 0.32). Notable findings on multivariate analysis include an association between shorter DSS and the following characteristics: (1) diagnosis from 1992-2004, (2) advanced age (80+), and (3) absence of cytoreductive nephrectomy. CONCLUSIONS: These data reflect progress in the management of mRCC, specifically in the era of targeted therapies. Notably, it was inferred that certain treatment strategies were employed during pre-specified time periods, representing a major caveat of the current analysis. Further studies related to the influence of age and race/ethnicity are warranted, as are studies exploring the role of cytoreductive nephrectomy and novel treatments for non-clear cell disease.

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[998]
TÍTULO / TITLE: - Docetaxel chemotherapy for Chinese patients with castrate-resistant prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

●●Enlace al texto completo (gratuito o de pago) 12809/hkmj133804
AUTORES / AUTHORS: - Cheung FY; Leung KC; Ngan RK
INSTITUCIÓN / INSTITUTION: - Department of Clinical Oncology, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong.
RESUMEN / SUMMARY: - OBJECTIVE. To determine the effectiveness and toxicity of docetaxel for Chinese patients with castrate-resistant prostate cancer in a local Hong Kong hospital. DESIGN. Case series. SETTING. A tertiary cancer centre in Hong Kong. PATIENTS. In all, 39 castrate-resistant prostate cancer patients were treated with 3-weekly docetaxel at 75 mg/m2 and prednisolone 10 mg daily between January 2006 and December 2011 in Queen Elizabeth Hospital. MAIN OUTCOME MEASURES. Prostate-specific antigen control rate, pain control rate, progression-free survival, overall survival, and complication rates. RESULTS. The prostate-specific antigen response rate was 36%, and 27 (69%) of the patients had improved pain control after chemotherapy. The median progression-free survival, cancer-specific survival,
and overall survival was 7.8 (95% confidence interval, 4.9-10.8) months, 13.0 (95% confidence interval, 9.6-16.3) months, and 12.2 (95% confidence interval, 9.3-15.1) months, respectively. The grade 3 anaemia and thrombocytopenia rates were 5%, and the neutropenic fever rate was 8%. CONCLUSIONS. Chemotherapy with docetaxel at a dose of 75 mg/m2 given once every 3 weeks together with daily prednisolone is well tolerated in Chinese and can offer good symptom palliation in suitable patients with castrate-resistant prostate cancer.
RESUMEN / SUMMARY: - BACKGROUND: Podocyte injury is an early feature of diabetic nephropathy (DN). Recently, urinary exosomal Wilm’s tumor-1 protein (WT1), shed by renal epithelial cells, has been proposed as a novel biomarker for podocyte injury. However, its usefulness as biomarker for early diabetic nephropathy has not been verified yet. We investigated urinary exosomal WT1 in type-1 diabetic patients to confirm its role as a non-invasive biomarker for predicting early renal function decline. METHODS: The expression of WT1 protein in urinary exosomes from spot urine samples of type-1 diabetes mellitus patients (n = 48) and healthy controls (n = 25) were analyzed. Patients were divided based on their urinary albumin excretion, ACR (mg/g creatinine) into non-proteinuria group (ACR<30 mg/g, n = 30) and proteinuria group (ACR>30 mg/g, n = 18). Regression analysis was used to assess the association between urinary exosomal levels of WT1 with parameters for renal function. Receiver Operating Characteristic (ROC) curve analysis was used to determine the diagnostic performance of exosomal WT1. RESULTS: WT1 protein was detected in 33 out of 48 diabetic patients and in only 1 healthy control. The levels of urinary exosomal WT1 protein is significantly higher (p = 0.001) in patients with proteinuria than in those without proteinuria. In addition, all the patients with proteinuria but only half of the patients without proteinuria were positive for exosomal WT1. We found that the level of exosomal WT1 were associated with a significant increase in urine protein-to-creatinine ratio, albumin-to-creatinine ratio, and serum creatinine as well as a decline in eGFR. Furthermore, patients exhibiting WT1-positive urinary exosomes had decreased renal function compared to WT1-negative patients. ROC analysis shows that WT-1 effectively predict GFR<60 ml. min⁻¹/1.73 m². CONCLUSION: The predominant presence of WT1 protein in urinary exosomes of diabetic patients and increase in its expression level with decline in renal function suggest that it could be useful as early non-invasive marker for diabetic nephropathy.
OBJECTIVE: To investigate the efficacy and safety of the treatment of the newly diagnosed multiple myeloma (MM) with or without renal impairment receiving the therapy of bortezomib, dexamethasone plus thalidomide (BTD) regimen in order to analyze the effects of BTD regimen on the prognosis of the MM patients with renal impairment compared with the patients without renal impairment. METHODS: Seventy-two newly diagnosed MM patients entered into our study and all the patients belonged to International Stage System (ISS) 3 in which transplantation patients were excluded or the patients refused receiving transplantation therapy. According to the level of serum creatinine (Scr), the patients were divided into two groups including group 1 (n=42) (Scr <2 mg/dL) and group 2 (n=30) (Scr >/=2 mg/dL). All the patients received the therapy of BTD regimen as induction therapy, and the median treatment time was 5 (range, 2-8) cycles. The outcome was analyzed retrospectively. RESULTS: The overall remission (OR) rates were 81.0% (group 1) and 80.0% (group 2). There was no statistical difference between the two groups (P>0.05). In group 2, 10 patients (33.3%) got renal function reversal, 14 patients (46.7%) got improved renal function and the median time to renal function reversal was 1.4 (range, 0.7-3.0) months. Among 12 patients with hemodialysis at diagnosis, 8 patients got rid of hemodialysis after median 4 cycles of therapy (range, 3-6 cycles). After a median follow-up period of 16 (range, 2-31) months, 5 patients (11.9%) in group 1 died and 9 patients (30.0%) in group 2 died (P=0.056). The 2-year estimate of overall survival was 77.3% in group 1 and 63.8% in group 2, respectively (P=0.188). During a median follow-up time of 13.0 months (range, 2-25 months), 15 patients (35.7%) in group 1 progressed and 13 patients (43.3%) in group 2 progressed (P=0.513). The 2-year estimate of response duration was 50.6% in group 1 and 42.1% in group 2, respectively (P=1). The main toxicities in the two groups included thrombocytopenia, peripheral neuropathy (PN), infection, herpes zoster and so on. The incidence of grade 3 and 4 adverse events was low. CONCLUSIONS: BTD regimen may become the front-line therapy for the newly diagnosed MM patients with renal impairment because BTD regimen can improve the prognosis of the patients with renal impairment as good as the patients without renal impairment.

[1002]
Axitinib Controlled Metastatic Renal Cell Carcinoma for 5 Years.

We present two patients with a long-term response to axitinib for cytokine-refractory metastatic renal cell carcinoma. One patient has had a continuing partial response for 58 months with cytokine-intolerant metastatic renal cell carcinoma and the other patient has had continuing stable disease accompanied by a mixed response for 57 months with cytokine-refractory and intolerant metastatic renal cell carcinoma. The condition of hypertension as an adverse event markedly depended on whether or not axitinib was administered. The patients responded to axitinib with an elevation of diastolic blood pressure to 90 mmHg or higher until 2 weeks after starting axitinib. To get a long-term response to axitinib, it may be important to control well the balance between treatment effect and adverse events while using drug withdrawal.

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Therapeutic Potential of an Anti-diabetic Drug, Metformin: Alteration of miRNA expression in Prostate Cancer Cells.

Background and Aims: Prostate cancer is the most commonly diagnosed cancer in males in many populations. Metformin is the most widely used anti-diabetic drug in the world, and there is increasing evidence of a potential efficacy of this agent as an anti-cancer drug. Metformin inhibits the proliferation of a range of cancer cells including prostate, colon, breast, ovarian, and glioma lines. MicroRNAs (miRNAs) are a class of small, non-coding, single-stranded RNAs that downregulate gene expression. We aimed to evaluate the effects of metformin treatment on changes in miRNA expression in PC-3 cells, and possible associations with biological behaviour. Materials and Methods: Average cell viability and cytotoxic effects of metformin were investigated at 24 hour intervals for three days using the xCELLigence system. The IC50 dose of metformin in the PC-3 cells was found to be 5 mM. RNA samples were used for analysis using custom multi-species microarrays.
containing 1209 probes covering 1221 human mature microRNAs present in miRBase 16.0 database. Results: Among the human miRNAs investigated by the arrays, 10 miRNAs were up-regulated and 12 miRNAs were down-regulated in the metformin-treated group as compared to the control group. In conclusion, expression changes in miRNAs of miR-146\(^\#\), miR-100, miR-425, miR-193\(^\#\)-3p and, miR-106b in metformin-treated cells may be important. This study may emphasize a new role of metformin on the regulation of miRNAs in prostate cancer.

[1004]
**TÍTULO / TITLE:** - Epithelioid angiomyolipoma of the kidney: Radiological imaging.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** - Tsukada J; Jinzaki M; Yao M; Nagashima Y; Mikami S; Yashiro H; Nozaki M; Mizuno R; Oya M; Kuribayashi S
**INSTITUCIÓN / INSTITUTION:** - Department of Diagnostic Radiology, Keio University School of Medicine, Tokyo.
**RESUMEN / SUMMARY:** - OBJECTIVES: To review the imaging findings of renal epithelioid angiomyolipomas. METHODS: Eight patients treated at two institutions were pathologically diagnosed as having epithelioid angiomyolipoma. All of them underwent computed tomography, and four underwent magnetic resonance imaging. The tumor size, existence of fat, heterogeneity, computed tomography attenuation, degree of enhancement, enhancement pattern and magnetic resonance imaging signal intensity were evaluated. RESULTS: Intratumoral fat was not detected in any of the cases. On unenhanced computed tomography, the intratumoral attenuation was hyperattenuating in six of the seven patients who were examined using this modality. On T2-weighted images, the signal intensity of the solid component, cyst wall or septum was low in three of the four cases. Four of the eight cases were heterogeneous solid-type accompanied by hemorrhage, necrosis or hyalinization. One homogeneous solid-type lesion was large in size and was pathologically accompanied by neither hemorrhage nor necrosis. All three multilocular cystic types were pathologically accompanied by massive hemorrhage in the cystic component. One was accompanied by spontaneous perirenal hematoma. CONCLUSIONS: The radiological appearance of most epithelioid angiomyolipomas has a tendency to be hyperattenuating on unenhanced computed tomography images, with low intensities on T2-weighted images. They can be heterogeneously solid, homogeneously solid or a multilocular cystic lesion with massive hemorrhage.
TÍTULO / TITLE: - Expression of the IAP protein family acts cooperatively to predict prognosis in human bladder cancer patients.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Chen X; Wang T; Yang D; Wang J; Li X; He Z; Chen F; Che X; Song X

INSTITUCIÓN / INSTITUTION: - Department of Urology, First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning 116011, P.R. China.

RESUMEN / SUMMARY: - The inhibitors of apoptosis (IAPs) are a group of anti-apoptotic factors in the apoptotic pathway that render cancer cells insensitive to apoptotic stimulation. Recently, several members of the IAP family have been investigated in the context of bladder cancer, and some of these have been associated with specific clinical and pathological tumor features, and with prognosis. These data suggested that the expression of an individual nuclear IAP has an important relationship with the progression of bladder cancer. To date, there are no studies concerning the overall tendencies of IAPs and their comparative therapeutic values in bladder cancer. In this study, we investigated the overall expression trends of the five tumor-related proteins, Survivin, cIAP1, cIAP2, XIAP and Livin, in normal bladder tissues and bladder cancer tissues. We classified and compared the gene expression data of these IAPs with the corresponding clinical and pathological tumor features, and with prognosis, in the development and progression of bladder cancer. The differences in IAP expression levels between archival bladder specimens from 36 normal controls and 105 patients who underwent surgery at our facility were examined using western blot analysis. The localization and expression level of each protein in low- and high-grade bladder cancer tissues were examined through immunohistochemistry. The cytoplasmic expression levels of each protein were scored as 0 (negative), +1 (weak), +2 (medium) or +3 (strong). The nuclear expression levels of cIAP1 and Survivin were scored as 0 (0%), +1 (1-25%), +2 (26-50%) or +3 (>50%). The results demonstrated that the expression of IAPs acted cooperatively to predict prognosis in human bladder cancer patients.

TÍTULO / TITLE: - Disappearance of a major thrombus in the brachiocephalic vein without anticoagulant therapy in a patient with seminoma: A case report.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Hongo H; Ide H; Hoshino K; Yasumizu Y; Uchida Y; Masuda T
INSTITUCIÓN / INSTITUTION: - Saitama Municipal Hospital, Department of Urology, Saitama Municipal Hospital, Mimuro, Midori-ku, Saitama City, Saitama, Japan.
RESUMEN / SUMMARY: - This is the first case report describing brachiocephalic vein thrombosis without compression by a metastatic tumour during chemotherapy for testicular cancer. According to previous reports of testicular cancer patients with a major thrombus, anticoagulant therapy was required to resolve all cases. However, in the present case, a major thrombus in the brachiocephalic vein disappeared without anticoagulant therapy. This 42-year-old man was diagnosed with testicular seminoma and multiple metastases to the para-aortic lymph nodes. After 3 cycles of cisplatin, etoposide and bleomycin (PEB) therapy, a major thrombus in the right brachiocephalic vein was recognized on a computed tomography (CT) scan. Although no anticoagulant therapy was undertaken, the thrombus in the right brachiocephalic vein was no longer visible on CT after the fourth cycle of PEB therapy.

[1007]
TÍTULO / TITLE: - Quality improvements in prostate radiotherapy: outcomes and impact of comprehensive quality assurance during the TROG 03.04 ‘RADAR’ trial.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kearvell R; Haworth A; Ebert MA; Murray J; Hooton B; Richardson S; Joseph DJ; Lamb D; Spry NA; Duchesne G; Denham JW
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia.
RESUMEN / SUMMARY: - INTRODUCTION: The Trans-Tasman Radiation Oncology Group 03.04 ‘Randomised Androgen Deprivation and Radiotherapy’ multicentre prostate cancer trial examined the optimal duration of androgen deprivation in combination with dose-escalated radiotherapy. Rigorous quality assurance (QA) processes were undertaken to ensure the validity and reliability of the radiation therapy treatment plan data. METHOD: QA processes included a planning benchmarking exercise and a periodic audit of target and normal tissue delineation. Centralised electronic review of digital plan data for external-beam radiotherapy was undertaken to detect protocol variations. The impact of clinical factors and feedback to submitting centres during the trial on variation rates was investigated. RESULTS: Twenty-three centres across Australia and New Zealand recruited 1071 participants to the trial. Treatment plans for 754
participants receiving external-beam treatment alone were reviewed. From these, 1185 minor and 86 major variations were identified, leading to feedback to treating centres to reduce variations for subsequent patients' treatment and plans, suggesting improvement in treatment quality through these QA programs. Participant anatomical factors (delineated clinical target volume and rectal volume) and treatment planning factors (beam energy, beam definition and patient position orientation) were found to significantly impact variation rates. The dummy run demonstrated disagreement in identification of the base of the prostate and the superior extent of the rectum. Feedback from the periodic audit led to a change of practice at five contributing centres.

CONCLUSION: The application of a suite of complementary QA activities allows the quality of trial data to be optimised and quantified, and can provide a catalyst for reforming treatment practices.

[1008]
TÍTULO / TITLE: - Giant renal oncocytoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.lpm.2012.11.023
AUTORES / AUTHORS: - Ilyass Addourouj M; Hamdoune A; Elondou JC; Ameur A; Abarr M
INSTITUCIÓN / INSTITUTION: - Mohammed V Military Teaching Hospital, Department of Urology, Rabat, Morocco. Electronic address: medil84@hotmail.fr.

[1009]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1093/jrr/rrt049
AUTORES / AUTHORS: - Shinohara N; Maruyama S; Shimizu S; Nishioka K; Abe T; C-Hatanaka K; Oba K; Nonomura K; Shirato H
INSTITUCIÓN / INSTITUTION: - Department of Renal and Genitourinary Surgery, Hokkaido University Graduate School of Medicine, North-15, West-7, Kitaku, Sapporo 060-8638, Japan.
RESUMEN / SUMMARY: - The purpose of this study was to compare the quality of life (QOL) in patients with localized prostate cancer (PC) after intensity-modulated radiation therapy assisted with a fluoroscopic real-time intensity-modulated radiation therapy (RT-IMRT) tumor-tracking system versus the QOL
after radical prostatectomy (RP). Between 2003 and 2006, 71 patients were enrolled in this longitudinal prospective study. Each patient was allowed to decide which treatment modality they would receive. Of the 71 patients, 23 patients underwent RT-IMRT, while 48 opted for RP. No patient received neo-adjuvant or adjuvant hormone therapy. The global QOL and disease-specific-QOL were evaluated before treatment and again at 1, 3 and 5 years after treatment. There was no significant difference in the background characteristics between the two groups. The 5-year biochemical progression-free survival was 90% in the RT-IMRT and 79% in the RP group. In the RT-IMRT group, there was no significant deterioration of the global QOL or disease-specific QOL through 5 years post-treatment. In the RP group, the urinary function, sexual function, and sexual bother indicators significantly deteriorated after treatment. Urinary and sexual function was significantly better in the RT-IMRT group at 1, 3 and 5 years post-treatment compared to the RP group. RT-IMRT may be a preferable treatment for localized PC because of similar efficacy to RP but better post-treatment QOL.

[1010]

TÍTULO / TITLE: - Preventive effects of monascus on androgen-related diseases: androgenetic alopecia, benign prostatic hyperplasia, and prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Chiu HW; Chen MH; Fang WH; Hung CM; Chen YL; Wu MD; Yuan GF; Wu MJ; Wang YJ
INSTITUCIÓN / INSTITUTION: - Department of Environmental and Occupational Health, National Cheng Kung University Medical College, Tainan, Taiwan.
RESUMEN / SUMMARY: - Androgen-related diseases impair the well-being of many aging men. Unfortunately, the medications used to treat these diseases have many side effects. Therefore, there is a significant need for the development of novel drugs to treat androgen-related diseases. In this study, we investigated the effects of Monascus cursory extraction (M-CE) on androgen-related diseases, including androgenetic alopecia (AGA), benign prostatic hyperplasia (BPH) and prostate cancer. We found that M-CE suppressed baldness in male B6CBAF1/j mice. Furthermore, M-CE decreased PSA levels, indicating a protective effect of M-CE on testosterone-induced hyperplasia. M-CE also significantly decreased tumor volume and tumor incidence in an N-methyl-N-nitrosourea (MNU)/testosterone-induced rat prostate cancer model and markedly decreased dihydrotestosterone (DHT) but not testosterone. Additionally, PCNA expression was decreased in the prostate of rats treated with M-CE. These results suggest that M-CE could be a new potential therapeutic candidate for the treatment of androgen-related diseases.
[1011]
TÍTULO / TITLE: - Preoperative levels of matrix metalloproteinase-7 and -9 and tissue inhibitor of matrix metalloproteinase-1 relation to pathologic parameters in bladder carcinoma patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Gunes M; Kemik AS; Pirincci N; Gecit I; Taken K; Yuksel MB; Kaba M; Eryilmaz R
INSTITUCIÓN / INSTITUTION: - Department of Urology, Yuzuncu Yil University Medical Faculty, Van, Turkey E-mail: drmustafa23@yahoo.com.
RESUMEN / SUMMARY: - Our aim was to test the hypothesis that preoperative serum levels of matrix metalloproteinase-7 (MMP-7) and -9 (MMP-9) and tissue inhibitor of matrix metalloproteinase (TIMP-1) levels correlate with pathological features. Serum levels of MMP-7, and MMP-9 and TIMP-1 were determined in 90 bladder cancer patients and 40 healthy controls using an enzyme linked immunosorbent assay. Preoperative serum MMP-7 and MMP-9 levels were significantly higher in cancer patients than control groups (p<0.001). In contrast, serum TIMP-1 levels were lower (p<0.001). Alteration in MMP-7, and MMP-9, and TIMP-1 production may contribute to tumor angiogenesis and be associated with clinic-pathological features.

[1012]
TÍTULO / TITLE: - Bilateral synchronous multifocal renal clear-cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Pothen L; Rouviere H; Bou Sleiman W; Aydin S; Feyaerts A; Nica MI; Lambert M
INSTITUCIÓN / INSTITUTION: - Service de Medecine Interne Generale, Cliniques Universitaires Saint Luc, Bruxelles, Belgium.

[1013]
TÍTULO / TITLE: - Sequencing CTLA-4 blockade with cell-based immunotherapy for prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1186/1479-5876-11-89
Resumen / Summary:

Background: The FDA recently approved an anti-CTLA-4 antibody (Ipilimumab) for the treatment of metastatic melanoma. This decision was based on Phase III results, which demonstrate that blocking this immune checkpoint provides a survival advantage in patients with advanced disease. As a single agent, ipilimumab is also being clinically evaluated in advanced (metastatic, castrate-resistant) prostate cancer and two randomized, placebo-controlled Phase III studies have recently completed accrual.

Methods: We used a well-described genetically engineered mouse (GEM), autochronous prostate cancer model (Pro-TRAMP) to explore the relative sequencing and dosing of anti-CTLA-4 antibody when combined with a cell-based, GM-CSF-secreting vaccine (GVAX). Results: Our results show that combined treatment results in a dramatic increase in effector CD8 T cells in the prostate gland, and enhanced tumor-antigen directed lytic function. These effects are maximized when CTLA-4 blockade is applied after, but not before, vaccination. Additional experiments, using models of metastatic disease, show that incorporation of low-dose cyclophosphamide into this combined treatment regimen results in an additional pre-clinical benefit. Conclusions: Together these studies define a combination regimen using anti-CTLA-4/GVAX immunotherapy and low-dose chemotherapy for potential translation to a clinical trial setting.

Titulo / Title:

Differential expression of prognostic proteomic markers in primary tumour, venous tumour thrombus and metastatic renal cell cancer tissue and correlation with patient outcome.

Resumen / Summary:

Renal cell carcinoma (RCC) is the most deadly of urological malignancies. Metastatic disease affects one third of patients at
diagnosis with a further third developing metastatic disease after extirpative surgery. Heterogeneity in the clinical course ensures predicting metastasis is notoriously difficult, despite the routine use of prognostic clinico-pathological parameters in risk stratification. With greater understanding of pathways involved in disease pathogenesis, a number of biomarkers have been shown to have prognostic significance, including Ki67, p53, vascular endothelial growth factor receptor 1 (VEGFR1) and ligand D (VEGFD), SNAIL and SLUG.

Previous pathway analysis has been from study of the primary tumour, with little attention to the metastatic tumours which are the focus of targeted molecular therapies. As such, in this study a tissue microarray from 177 patients with primary renal tumour, renal vein tumour thrombus and/or RCC metastasis has been created and used with Automated Quantitative Analysis (AQUA) of immunofluorescence to study the prognostic significance of these markers in locally advanced and metastatic disease. Furthermore, this has allowed assessment of differential protein expression between the primary tumours, renal vein tumour thrombi and metastases. The results demonstrate that clinico-pathological parameters remain the most significant predictors of cancer specific survival; however, high VEGFR1 or VEGFD can predict poor cancer specific survival on univariate analysis for locally advanced and metastatic disease. There was significantly greater expression of Ki67, p53, VEGFR1, SLUG and SNAIL in the metastases compared with the primary tumours and renal vein tumour thrombi. With the exception of p53, these differences in protein expression have not been shown previously in RCC. This confirms the importance of proliferation, angiogenesis and epithelial to mesenchymal transition in the pathogenesis and metastasis of RCC. Importantly, this work highlights the need for further pathway analysis of metastatic tumours for overcoming drug resistance and developing new therapies.

[1015]

**TÍTULO / TITLE:** - Phase II Study of Satraplatin and Prednisone in Patients With Metastatic Castration-Resistant Prostate Cancer: A Pharmacogenetic Assessment of Outcome and Toxicity.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

- Enlace al texto completo (gratuito o de pago) 1016/j.clgc.2013.04.007

**AUTORES / AUTHORS:** - Figg WD; Chau CH; Madan RA; Gulley JL; Gao R; Sissung TM; Spencer S; Beatson M; Aragon-Ching J; Steinberg SM; Dahut WL

**INSTITUCIÓN / INSTITUTION:** - Medical Oncology Branch, Center for Cancer Research (CCR), National Cancer Institute (NCI), National Institutes of Health (NIH), Bethesda, MD. Electronic address: figgw@helix.nih.gov.

**RESUMEN / SUMMARY:** - BACKGROUND: We assessed the effect of excision repair cross-complementing group 1 (ERCC1) and x-ray cross-complementing
group 1 (XRCC1) gene polymorphisms on treatment outcomes with satraplatin and prednisone in patients with metastatic castration-resistant prostate cancer previously treated with docetaxel-based therapy. PATIENTS AND METHODS: Twenty-four patients were enrolled in this single-arm study. The primary objective was to determine if the presence of ERCC1 Asn118Asn (N118N, 500C>T, rs11615) and XRCC1 Arg399Gln (R399Q, 1301G>A, rs25487) genetic variants might be associated with an impact on progression-free survival (PFS); secondary objectives included overall response, survival, and toxicity. RESULTS: After population stratification by race, white patients carrying heterozygous or variant genotypes at the ERCC1 C>T locus had a >3-fold longer median PFS (5.8 vs. 1.8 months; 2P = .18, adjusted) and 5-fold longer median overall survival (OS) (15.7 vs. 3.2 months; 2P = .010, adjusted) than did patients carrying only wild-type alleles. For the XRCC1 G>A variant, without regard to race, patients carrying the wild-type GG alleles had a longer PFS (9.3 months) than those carrying GA or AA alleles (2.7 months; 2P = .02). Similarly, those carrying GG alleles did not reach median OS, whereas those carrying GA or AA alleles had a median OS of 9.6 months (2P = .12, adjusted). Multivariable analysis by using Cox proportional hazards modeling demonstrated that only XRCC1 was associated with PFS. CONCLUSIONS: To our knowledge, this is the first prospective study to date in patients with metastatic castration-resistant prostate cancer that describes predictive germline polymorphisms of ERCC1 and XRCC1 for assessing the clinical activity of satraplatin.

[1016]

**TÍTULO / TITLE:** Safety of megestrol acetate in palliating anorexia-cachexia syndrome in patients with castration-resistant prostate cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Hong S; Jeong IG; You D; Lee JL; Hong JH; Ahn H; Kim CS

**INSTITUCIÓN / INSTITUTION:** Department of Urology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea.

**RESUMEN / SUMMARY:** There are concerns whether megestrol acetate (MA) stimulates the growth of prostate cancer in castration-resistant prostate cancer (CRPC). We evaluated the effect of cumulative doses of MA on the disease-specific survival (DSS) in patients with CRPC who were receiving Docetaxel-based chemotherapy. From July 2003 through June 2009, we identified 109 consecutive patients with CRPC and who had received docetaxel-based chemotherapy. Of these patients, 68 (62.4%) have not received MA, whereas
21 patients (19.3%) and 20 patients (18.3%) had received low dose MA (total \( \leq 18,400 \text{ mg} \)) and high dose MA (total > 18,400 mg), respectively. We assessed the effect of several variables on DSS. None of the clinicopathological variables differed among the three groups. When comparing DSS using Kaplan-Meier analysis, there was no statistically significant survival differences among the three groups (\( P = 0.546 \)). Using multivariate Cox proportional analyses with backward elimination, the number of docetaxel cycles was only significant factor predicting DSS (HR: 0.578, 95% CI: 0.318-0.923, \( P = 0.016 \)). Cumulative doses of MA as adjuvant treatment for patients with CRPC and who are receiving docetaxel-based chemotherapy, did not affect their DSS. Therefore, MA can be safely administered in cachexic patients with CRPC.

[1017]
TÍTULO / TITLE: - Glans reconstruction with the use of an inverted urethral flap after distal penile amputation for carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Sansalone S; Garaffa G; Vespasiani G; Zucchi A; Kuehhas FE; Herwig R; Silvani M; Pecoraro S; Loreto C; Leonard R
INSTITUCIÓN / INSTITUTION: - Department of Experimental Medicine and Surgery, Tor Vergata University of Rome, Rome. salvatore.sansalone@yahoo.it.
RESUMEN / SUMMARY: - Restoration of adequate cosmesis and preservation of sexual and urinary function are the main goals of penile reconstructive surgery following amputation for carcinoma. Split thickness skin grafts and oral mucosa grafts have been widely used for the creation of a pseudoglans with excellent cosmetic and functional results. The main drawbacks associated with the use of grafts are donor site morbidity, the lack of engorgement of the pseudoglans and the risk of poor graft take, which may lead to contracture and poor cosmetic results. In the present series the long term cosmetic and functional outcomes of glans reconstruction with an inverted distal urethral flap are described.

[1018]
TÍTULO / TITLE: - Cost-effectiveness analysis comparing degarelix with leuprolide in hormonal therapy for patients with locally advanced prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
 ● Enlace al texto completo (gratis o de pago) 1586/erp.13.13
Degarelix, approved in the USA in 2008, is a gonadotropin-releasing hormone antagonist, representing one of the latest additions to androgen deprivation therapy (ADT). ADT is used as first-line therapy for locally advanced or metastatic prostate cancer with the aim to reduce testosterone to castrate levels. Like other gonadotropin-releasing hormone-antagonists, degarelix treatment results in rapid decrease in luteinizing hormone, follicle-stimulating hormone and testosterone levels without the associated risk of flare. Using one registration trial for degarelix with leuprolide as the active control, a cost-effectiveness analysis with a Markov model and a 20-year time horizon found the incremental cost-effectiveness ratio for degarelix to be US$245/quality-adjusted life years. Degarelix provides a cost-effective treatment for ADT among patients with locally advanced prostate cancer.

[1019]

Plasma Vascular Endothelial Growth Factors A and C in Patients undergoing Prostatic Biopsy and TURP for Suspected Prostatic Neoplasia.

Background: Formation of new blood vessels is necessary for the development and spread of neoplasms more than 1 mm3 in volume, angiogenesis being responsible for formation of new from pre-existing blood vessels. Vascular endothelial growth factor (VEGF) is pivotal and the best studied angiogenic factor in all human cancers. Therefore we designed this study to investigate the role of VEGF-A and VEGF-C in prostate cancer in comparison with BPH controls in a north Indian population. Methods: In this case-control study a total of 100 subjects were included on the basis of confirmed histopathological reports, out of which 50 were prostate cancer patients and the other 50 were BPH patients with PSA levels >2 ng/ml and abnormal digital rectal examination (DRE) findings during September 2009 to August 2011 from the Department of Urology, KGMU, Lucknow, India. Plasma levels of VEGF were determined using quantitative immunoassay (ELISA-enzyme linked immunosorbent assay). Statistical analysis was carried out using SPSS 15.0 version. Results: The mean age of prostate cancer (67.6+/-.572)
patients was significantly higher (p=0.005) than BPH (63.6+/−7.92) patients. Expression of VEGF-A was not significantly higher in disease stage C1 than D1 or D2 and A or B (p=0.13) while the level of VEGF-A was significantly higher (p=0.04) in prostate cancer as compared to BPH subjects (PCa=13.0 pg/ml, BPH=6.8 pg/ml). Levels of VEGF-C were similar in both groups (PCa=832.6 pg/ml, BPH=823.7 pg/ml). In ROC curve, the area under curve (AUC) was 0.70 (95%CI: 0.60-0.80) and the cut-off value for which a higher proportion of patients was correctly classified (20%) was 26.0 pg/mL. Conclusion: Although VEGF-A is increased in cancer prostate patients a statistically significant correlation could not be established in this study. VEGF-C was not found to be a useful biomarker.

[1020]

**TÍTULO / TITLE:** Contrast-enhanced transrectal ultrasonography: Measurement of prostate cancer tumor size and correlation with radical prostatectomy specimens.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Qi TY; Chen YQ; Jiang J; Zhu YK; Yao XH; Qi J

**INSTITUCIÓN / INSTITUTION:** Department of Ultrasonography, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China.

**RESUMEN / SUMMARY:** OBJECTIVES: To determine the accuracy of contrast-enhanced transrectal ultrasonography for tumor size measurements of hypoechoic prostate cancer foci located in the peripheral zone. METHODS: A total of 55 men scheduled for radical prostatectomy, with biopsy-proven cancer in hypoechoic foci located in the peripheral zone, were consecutively enrolled in the present prospective study. Each patient underwent grayscale ultrasound and contrast-enhanced transrectal ultrasonography of the prostate according to a standardized protocol. The maximum tumor diameter on grayscale imaging and contrast-enhanced transrectal ultrasonography was compared with that determined using histopathology. RESULTS: A mean underestimation was documented to be approximately 3.9 mm and 0.6 mm for grayscale and contrast-enhanced transrectal ultrasonography imaging, respectively. Grayscale and contrast-enhanced transrectal ultrasonography imaging underestimated measurements by 76.67% (46 of 60) and 48.33% (29 of 60), whereas overestimated measurements were 20% (12 of 60) and 26.67% (16 of 60), respectively. A strong correlation was observed between contrast-enhanced transrectal ultrasonography and histopathological measurements (r = 0.91, P < 0.0001). A weak linear correlation was found between grayscale and histopathological measurements (r = 0.59, P < 0.0001). Bland-Altman analysis results were in complete accordance with correlation analysis results. For cases
with maximum histopathological tumor diameters ≤10 mm and >10 mm, 40% (6 of 15) and 86.67% (39 of 45) were index tumors, respectively (P < 0.0001).

CONCLUSIONS: Contrast-enhanced transrectal ultrasonography is significantly more accurate than conventional grayscale imaging for measuring prostate tumor size, especially for tumors with a diameter >10 mm, and it might have a role in preoperative assessment of prostatic index tumor sizes.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Yamamoto T
INSTITUCIÓN / INSTITUTION: - Department of Urology, Nagoya University Graduate School of Medicine, Nagoya, Japan. toku@med.nagoya-u.ac.jp.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Eilat-Tsanani S; Tabenkin H; Shental J; Elmalah I; Steinmetz D
INSTITUCIÓN / INSTITUTION: - Department of Family Medicine, HaEmek Medical Center, Afula, Israel. eilat@clalit.org.il
RESUMEN / SUMMARY: - BACKGROUND: Radical prostatectomy is one option for treating localized prostate cancer, but it can cause functional impairment of the urogenital system. OBJECTIVES: To describe the outcomes of radical prostatectomy as perceived by the patients, and their ways of coping with them. METHODS: We conducted a qualitative study of 22 men with localized prostatic cancer 1 year after surgery. The key questions related to the effect of the disease and the surgery on their lives and their view on the value of the surgery. RESULTS: The surgery was perceived as a necessary solution for the diagnosed cancer. All the participants suffered from varying degrees of urinary incontinence and erectile dysfunction. Urinary incontinence caused severe suffering. The impaired sexual ability affected relations with partners and led to feelings of shame and guilt and a decreased sense of self-esteem. In retrospect, the participants still viewed the surgery as a life-saving procedure. Faith in the surgeon contributed to their affirmation of the decision to undergo
surgery despite the difficulties. CONCLUSIONS: Patients were prepared to suffer the inevitable physical and psychological sequelae of radical prostatectomy because they believed the surgery to be a definitive solution for cancer. Surgeons advising patients with localized prostatic cancer on treatment options should address these difficult issues and provide psychological support, either themselves or in collaboration with professionals.

[1023]
TITULO / TITLE: SATB1 is overexpressed in metastatic prostate cancer and promotes prostate cancer cell growth and invasion.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

[Enlace al texto completo (gratuito o de pago) 1186/1479-5876-11-111]
AUTORES / AUTHORS: Mao L; Yang C; Wang J; Li W; Wen R; Chen J; Zheng J
INSTITUCIÓN / INSTITUTION: Jiangsu Key Laboratory of Biological Cancer Therapy, Xuzhou Medical College, Xuzhou, 221002, China.
maolijunxz@163.com.
RESUMEN / SUMMARY: BACKGROUND: Special AT-rich sequence binding protein 1 (SATB1) is a nuclear factor that functions as the global chromatin organizer to regulate chromatin structure and gene expression gene expression. SATB1 has been shown to be abnormally expressed in various types of cancer. However, the expression and role of SATB1 in prostate cancer remain unclear. METHODS: 120 cases of prostatic carcinoma and 60 cases of benign prostate hyperplasia were analyzed for SATB1 expression by immunohistochemistry. LNCaP, DU-145, and PC3 prostate cancer cells were examined for SATB1 expression by Western blot analysis. Cell proliferation and invasion was evaluated by CCK8 and transwell invasion assay, respectively. RESULTS: SATB1 staining was stronger in prostatic carcinomas with metastasis than in those without metastasis, but was absent in benign prostate hyperplasia. Furthermore, SATB1 expression was positively correlated with bone metastasis and the Gleason score. SATB1 overexpression promoted the proliferation and invasion of LNCaP cells while SATB1 knockdown inhibited the proliferation and invasion of DU-145 cells. CONCLUSIONS: These findings provide novel insight into oncogenic role of SATB1 in prostate cancer, suggesting that SATB1 is a promising biomarker and therapeutic target for prostate cancer.

[1024]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Shan J; Al-Rumaihi K; Rabah D; Al-Bozom I; Kizhakayil D; Farhat K; Al-Said S; Kfoury H; Dsouza SP; Rowe J; Khalak HG; Jafri S; Aigha II; Chouchane L

INSTITUCIÓN / INSTITUTION: - Laboratory of Genetic Medicine and Immunology, Weill Cornell Medical College in Qatar, Qatar Foundation, Doha, Qatar. loc2008@qatar-med.cornell.edu.

RESUMEN / SUMMARY: - BACKGROUND: Large databases focused on genetic susceptibility to prostate cancer have been accumulated from population studies of different ancestries, including Europeans and African-Americans. Arab populations, however, have been only rarely studied. METHODS: Using Affymetrix Genome-Wide Human SNP Array 6, we conducted a genome-wide association study (GWAS) in which 534,781 single nucleotide polymorphisms (SNPs) were genotyped in 221 Tunisians (90 prostate cancer patients and 131 age-matched healthy controls). TaqMan® SNP Genotyping Assays on 11 prostate cancer associated SNPs were performed in a distinct cohort of 337 individuals from Arab ancestry living in Qatar and Saudi Arabia (155 prostate cancer patients and 182 age-matched controls). In-silico expression quantitative trait locus (eQTL) analysis along with mRNA quantification of nearby genes was performed to identify loci potentially cis-regulated by the identified SNPs. RESULTS: Three chromosomal regions, encompassing 14 SNPs, are significantly associated with prostate cancer risk in the Tunisian population (P = 1 x 10^-4 to P = 1 x 10^-5). In addition to SNPs located on chromosome 17q21, previously found associated with prostate cancer in Western populations, two novel chromosomal regions are revealed on chromosome 9p24 and 22q13. eQTL analysis and mRNA quantification indicate that the prostate cancer associated SNPs of chromosome 17 could enhance the expression of STAT5B gene. CONCLUSION: Our findings, identifying novel GWAS prostate cancer susceptibility loci, indicate that prostate cancer genetic risk factors could be ethnic specific.

[1025]

TÍTULO / TITLE: - Editorial Comment from Dr Simmons to Prostate HistoScanning: A screening tool for prostate cancer?

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

Enlace al texto completo (gratuito o de pago) 1111/iju.12170
AUTORES / AUTHORS: - Simmons LA
INSTITUCIÓN / INSTITUTION: - Division of Surgery and Interventional Science, University College London, London, UK. lucy.simmons@doctors.org.uk.

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[1026]
TÍTULO / TITLE: - Editorial comment from Dr Salomon to Prostate HistoScanning: A screening tool for prostate cancer?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Salomon G
INSTITUCIÓN / INSTITUTION: - Martini Clinic, Prostate Cancer Center, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany. gsalomon@uke.uni-hamburg.de.

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[1027]
TÍTULO / TITLE: - Prostate HistoScanning: A screening tool for prostate cancer?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - De Coninck V; Braeckman J; Michielsen D
INSTITUCIÓN / INSTITUTION: - Department of Urology, UZ Brussel, Free University of Brussels, Brussels, Belgium.
RESUMEN / SUMMARY: - OBJECTIVE: To evaluate Prostate HistoScanning as a screening tool for prostate cancer in a pilot study. METHODS: During a 6-month period, 94 men with normal or suspicious digital rectal examination, normal or elevated prostate-specific antigen, or an increased prostate-specific antigen velocity were examined with Prostate HistoScanning. Based on these parameters and HistoScanning analysis, 41 men were referred for prostate biopsy under computer-aided ultrasonographic guidance. The number of random biopsy cores varied depending on the prostate volume. Targeted biopsies were taken in the case of computer-aided ultrasonographic area suspicious for malignancy. A logistic regression analysis was carried out to estimate the probability of resulting in a positive prostate biopsy based on the HistoScanning findings. RESULTS: Following a logistic regression analysis, after adjusting for age, digital rectal examination, serum prostate-specific antigen level, prostate volume and tumor lesion volume, every cancer volume increase of 1 mL estimated by HistoScanning was associated with a nearly threefold increase in the probability of resulting in a positive biopsy (odds ratio 2.9; 95% confidence interval 1.2-7.0; P-value 0.02). Prostate cancer was found
in 17 of 41 men (41%). In patients with cancer, computer-aided ultrasonography-guided biopsy was 4.5-fold more likely to detect cancer than random biopsy. The prostate cancer detection rate for random biopsy and directed biopsy was 13% and 58%, respectively. HistoScanning-guided biopsy significantly decreased the number of biopsies necessary (P-value <0.0001).

CONCLUSIONS: Our findings suggest that Prostate HistoScanning might be helpful for the selection of patients in whom prostate biopsies are necessary. This imaging technique can be used to direct biopsies in specific regions of the prostate with a higher cancer detection rate.

[1028]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Grasso M; Blanco S; Grasso AA; Nespoli L
INSTITUCIÓN / INSTITUTION: - Department of Urology, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Universita degli Studi di Milano, Milano. angelica_grasso@yahoo.it.
RESUMEN / SUMMARY: - We report the case of a patient who had undergone polypropylene plug placement 3 years before and referred to our institution with testicular tumor. CT scan demonstrated an enlargement of pelvic lymph nodes on the tumor side while retroperitoneal nodes were normal. Orchifunicolectomy was performed and histopathological examination showed a mixed germ cell tumor involving the tunica vaginalis, rete testis, epididymis and spermatic cord. After surgery the patient was addressed to adjuvant chemotherapy according to PEB scheme. Clinical re-staging showed a decrease of the pelvic bulk disease whereas retroperitoneal nodes were still normal and tumor markers were negative. Left external, internal and common iliac lymphadenectomy as well as left modified template nervesparing retroperitoneal lymph node dissection was performed. Intraoperatively the node bulk was firmly adherent to the external iliac artery and extended until the common iliac bifurcation. In the deeper part of this enlarged and firm lymphatic chain the polypropylene plug placed at the time of hernioplasty was found. Behind the plug all retroperitoneal nodes appeared normal and resulted negative on histopathologic examination. The patient had an unusual metastatization, probably due to the plug.

[1029]
TÍTULO / TITLE: - Excellent long time survival for Swedish patients starting home-hemodialysis with and without subsequent renal transplantations.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
- Enlace al texto completo (gratuito o de pago) 1111/hdi.12046
AUTORES / AUTHORS: - Rydell H; Krutzen L; Simonsen O; Clyne N; Segelmark M
INSTITUCIÓN / INSTITUTION: - Department of Nephrology and Transplantation, Skane University Hospital; Department of Clinical Sciences, Lund University, Lund.
RESUMEN / SUMMARY: - Survival for patients on dialysis is poor. Earlier reports have indicated that home-hemodialysis is associated with improved survival but most of the studies are old and report only short-time survival. The characteristics of patient populations are often incompletely described. In this study, we report long-term survival for patients starting home-hemodialysis as first treatment and estimate the impact on survival of age, comorbidity, decade of start of home-hemodialysis, sex, primary renal disease and subsequent renal transplantation. One hundred twenty-eight patients starting home-hemodialysis as first renal replacement therapy 1971-1998 in Lund were included. Data were collected from patient files, the Swedish Renal Registry and Swedish census. Survival analysis was made as intention-to-treat analysis (including survival after transplantation) and on-dialysis-treatment analysis with patients censored at the day of transplantation. Ten-, twenty- and thirty-year survival were 68%, 36% and 18%. Survival was significantly affected by comorbidity, age and what decade the patients started home-hemodialysis. For patients younger than 60 years and with no comorbidities, the corresponding figures were 75%, 47% and 23% and a subsequent renal transplantation did not significantly influence survival. Long-term survival for patients starting home-hemodialysis is good, and improves decade by decade. Survival is significantly affected by patient age and comorbidity, but the contribution of subsequent renal transplantation was not significant for younger patients without comorbidities.

[1030]
TÍTULO / TITLE: - The Dilemma of Localizing Disease Relapse After Radical Treatment for Prostate Cancer: Which is The Value of The Actual Imaging Techniques?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Schiavina R; Ceci F; Borghesi M; Brunocilla E; Vagnoni V; Gacci M; Castellucci P; Nanni C; Martorana G; Fanti S
INSTITUCIÓN / INSTITUTION: - Service of Nuclear Medicine, Deptment of Radiological and Histopathological Sciences, University of Bologna, S. Orsola-Malpighi Hospital Via Massarenti 9, 40138 Bologna, Italy. francesco.ceci83@gmail.com; francesco.ceci@studio.unibo.it.
RESUMEN / SUMMARY: - Only few patients with PSA relapse after radical treatment will show clinically detectable disease. Although the natural history of recurrent prostate cancer is often one of slowly progressing disease, in some men it can be rapid and may need a salvage treatment. In general, time to PSA relapse, PSA velocity and PSA doubling time are useful in patient assessment. In patients with PCa disease relapse after primary therapy, salvage treatment for a local recurrence should only be offered to patients with little risk of already having metastases. In these patients a systemic imaging negative for metastases is mandatory, a positive biopsy is not always necessary before radiotherapy, but is mandatory before salvage prostatectomy. In patients with a high risk of distant metastases and suitable for systemic salvage therapy, a positive lesion must be obviously visualized with one of the currently available imaging techniques. Transrectal ultrasound has low accuracy in the detection of the recurrence. Multiparametric Magnetic Resonance Imaging may have a role in the early phase of PSA relapse. Conventional imaging, such as bone scan and CT, are not suggested in the initial phase of BCR. Today, it has been reported that PET/CT allows changing the therapeutic strategy (from palliative to curative treatment and vice-versa) in about 20% of cases. In recent years, the new radiotracer 18F-FACBC has been proposed as a possible alternative radiopharmaceutical to detect PCa relapse. The aim of the present paper is to evaluate the management of patients with BCR after radical treatment of PCa from the urologist point of view.

[1031] TÍTULO / TITLE: - Treatment of upper urinary calculi with Chinese minimally invasive percutaneous nephrolithotomy: a single-center experience with 12,482 consecutive patients over 20 years.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Zeng G; Mai Z; Zhao Z; Li X; Zhong W; Yuan J; Wu K; Wu W

INSTITUCIÓN / INSTITUTION: - Department of Urology, Minimally Invasive Surgery Center, The First Affiliated Hospital of Guangzhou Medical University, 1# Kangda Road, Haizhu District, Guangzhou, 510230, China, gzgyzgh@vip.tom.com.
RESUMEN / SUMMARY: - The Chinese minimally invasive percutaneous nephrolithotomy (MPCNL) was a modified version of standard PCNL which utilizes smaller tract and sheaths. The aim of this study was to present our experience on its efficacy and safety, and to grade its complications according to the modified Clavien classification. Between 1992 and 2011, 12,482 patients
who underwent 13,984 MPCNL procedures entered this study. Data on stone size, access number, operative time, hospital length of stay, stone-free rate (SFR), and complications according to the modified clavien system were evaluated prospectively. Their mean age of patients was 47.6 years (range 0.6-93). The mean stone size was 3.2 +/- 0.8 (1.4-7.4) cm. The mean operative time was 83 +/- 38 min. Mean hemoglobin drop was 13.5 +/- 11.3 g/L. Mean hospital stay was 10.3 +/- 6.4 days (2-22 days). The initial SFR after first procedure was 78.6 %. In 14.7 % of cases with a second look, the SFR increase to 89.9 %. At 3 months after auxiliary procedures (re-PCNL, ureterorenoscopy, and shock wave lithotripsy), the overall SFR was achieved to 94.8 %. A total of 3,624 complications (25.92 %) were observed in 2,591 (18.53 %) procedures. There were 2,355 grade I (16.84 %), 706 grade II (5.05 %), 553 grade III (3.95 %), 7 grade IV (0.05 %), and three death of grade V (0.02 %) complications. This large-scale, contemporary analysis confirms MPCNL is still a safe and efficacious treatment option of kidney stones with a high stone-free rate and uncommon rate of high grade complications.

[1032]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ellett JD; Rosoff JS; Prasad SM
INSTITUCIÓN / INSTITUTION: - Department of Urology, Medical University of South Carolina, Charleston, SC 29425, USA.

[1033]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Karimpur-Zahmatkesh A; Farzaneh F; Pouresmaeili F; Hosseini J; Azarghashb E; Yaghoobi M
INSTITUCIÓN / INSTITUTION: - Medical Genetics Department, Shahid Beheshti of Medical Science University, Iran E-mail: farahzaneh@yahoo.com.
RESUMEN / SUMMARY: - Background: Studies have shown that alterations of steroid hormone metabolism, particularly involving testosterone, affect the risk of prostate cancer. Therefore, genetic variation in genes of enzymes which are involved could be of importance. The gene most interest is CYP17, whose enzyme product has an essential role in testosterone hormone synthesis. Some studies have indicated that the A2 allele polymorphism of CYP17 associated
with increased risk of prostate cancer that could be affected by ethnicity. Therefore, the aim of this study was determination of presence or absence of the A2 allele in patients with prostate cancer. Materials and Methods: We studied the association of A2 allele and prostate cancer among 74 patients with prostate cancer and 128 healthy men which were referred to hospitals of SBMU. Results: This study revealed a significant association between prostate cancer risk and the A2 allele in an Iranian population so that A1A2 and A2A2 genotypes were more common in cases than controls with P-values of 0.029 and 0.010, respectively. Conclusions: Results of our study support a possible role of the A2 allele in sporadic prostate cancer development in Iran, in line with findings elsewhere.

[1034]

**TITULO / TITLE:** - Unilateral renal artery stenosis with renal atrophy in a patient with metastatic papillary thyroid carcinoma treated with sorafenib.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - British Medical J (BMJ). Acceso gratuito al texto completo.

●●Enlace a la Editora de la Revista http://bmj.com/search.dtl


●●Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-009898

**AUTORES / AUTHORS:** - Shawa H; Busaidy NL; Schellingerhout D; Habra MA

**INSTITUCIÓN / INSTITUTION:** - Endocrine Neoplasia, MD Anderson Cancer Center, Houston, Texas, USA.

**RESUMEN / SUMMARY:** - Tyrosine kinase inhibitors (TKIs) have been recently introduced for treatment of different malignancies. Various cardiovascular toxicities have been reported with TKIs with hypertension being the most common adverse cardiovascular event. We report a case of a 60-year-old woman who developed left renal artery stenosis associated with renal atrophy in the context of metastatic papillary thyroid carcinoma treated with sorafenib. Renal atrophy was noticed during serial imaging studies to monitor cancer therapy. Clinically, she was asymptomatic without significant change in blood pressure. The glomerular filtration rate dropped from 88 ml/min/1.73 m(2) at baseline to 56 ml/min/1.73 ml/min and partially recovered to 71 ml/min/1.73 m(2) after renal artery stenting. To our knowledge, this will be the first known case of renal artery stenosis associated with TKI use. Physicians may need to investigate the possibility of developing renal artery stenosis in patients with unexplained worsening in kidney functions while on TKIs.

[1035]
TÍTULO / TITLE: - Impact of hospital volume on local recurrence and distant metastasis in bladder cancer patients treated with radical cystectomy in Sweden.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Sabir EF; Holmang S; Liedberg F; Ljungberg B; Malmstrom PU; Mansson W; Wijkstrom H; Jahnson S

INSTITUCIÓN / INSTITUTION: - Department of Urology, Institution for Medical Sciences, Linkoping University, Linkoping, Sweden.

RESUMEN / SUMMARY: - Abstract Objective. This study evaluated the impact of hospital volume on local recurrence and distant metastasis in a population-based series of radical cystectomy patients in Sweden. Material and methods. All patients who underwent cystectomy for bladder cancer in 1997-2002 in Sweden and were reported to the National Bladder Cancer Registry were included. A high-volume hospital (HVH) was defined as one with \( \geq 10 \) cystectomies/year and a low-volume hospital (LVH) as one with <10 cystectomies/year. Information on preoperative tumour, node, metastasis (TNM) classification, operative procedure, postoperative course and follow-up was obtained from medical records. Results. Of the 1126 patients, 827 (74%) were males. The mean age was 66 years and median follow-up 47 months. Of the 610 (54%) HVH patients, 68 (11%) were pT0, 123 (20%) < pT2, 177 (29%) pT2, 242 (40%) > pT2 and 69 (11%) were microscopic non-radical. Corresponding figures for the 516 (46%) LVH patients were 35 (7%), 68 (13%), 191 (37%), 222 (43%) and 96 (19%). Local recurrence was observed in 245 patients (22%): 113 (19%) at HVHs and 132 (26%) at LVHs. Distant metastasis was found in 363 (32%): 203 (33%) at HVHs and 160 (31%) at LVHs. Perioperative chemotherapy was given to 193 (17%). Multivariate Cox proportional hazards analysis showed that local recurrence was associated with LVHs and non-organ-confined disease, whereas distant metastasis was correlated with non-organ-confined disease and lymph-node metastases. Conclusions. In this retrospective analysis, local tumour recurrence after cystectomy was common, particularly in patients with non-organ-confined disease. Furthermore, local recurrence was more frequent at LVHs than HVHs, and overall survival was better at HVHs. These findings suggest that concentrating cystectomies in HVHs may improve outcomes such as local recurrence and overall survival.

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TÍTULO / TITLE: - Ki-67 proliferation index in renal biopsy samples of patients with systemic lupus erythematosus and its correlation with clinical findings.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Dalkilic E; Filiz G; Yavuz M; Dilek K; Ersoy A; Yurtkuran M; Oruc A; Gul CB; Gullulu M

INSTITUCIÓN / INSTITUTION: - Division of Rheumatology, Department of Internal Medicine, Uludag University Faculty of Medicine, Bursa, Turkey.
edizinci@hotmail.com.

RESUMEN / SUMMARY: - Introduction. Systemic lupus erythematosus is an autoimmune disease that may affect almost all organ systems. Renal involvement is the most significant prognostic factor. Renal biopsy findings play an important role in treatment decision. Ki-67 is a monoclonal antibody that is only found in proliferative cells. This study aimed to investigate the proliferative activity in renal biopsy specimens of patients with lupus nephritis using the Ki-67 monoclonal antibody, and to compare the proliferative index between different subgroups of patients. Materials and Methods. Renal biopsy specimens of 29 patients with systemic lupus erythematosus were retrospectively evaluated. Type of lupus nephritis and activity and chronicity indexes were determined. Ki-67 immunostaining was performed. For each patient, 1000 cells were counted and the number of Ki-67 positive cells was determined. The Ki-67 activity index was compared between different subgroups of lupus nephritis and correlated with systemic lupus erythematosus disease activity index, serum creatinine, proteinuria, anticardiolipin antibodies, and complement levels. Results. A positive correlation between Ki-67 proliferation index, serum creatinine levels, and systemic lupus erythematosus disease activity index were found. Although conventional activity indexes were low, in 3 of 9 patients with class II lupus nephritis, Ki-67 proliferation indexes were high, indicating proliferation. Conclusions. Ki-67 can be used as a proliferation marker in renal biopsy specimens for patients diagnosed with systemic lupus erythematosus.

[1037]

TÍTULO / TITLE: - Asp299Gly and Thr399Ile polymorphism of TLR-4 gene in patients with prostate cancer from North India.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Priyadarshini A; Chakraborti A; Mandal AK; Singh SK

INSTITUCIÓN / INSTITUTION: - Department of Experimental Medicine and Biotechnology, Post Graduate Institute of Medical Education and Research, Chandigarh, (UT), India.

RESUMEN / SUMMARY: - BACKGROUND: The etiological factors associated with prostate cancer (CaP) have not been completely understood as yet. Genetic predisposition and inflammation is fast emerging as risk factors for CaP is a key player in the innate immune response and plays role in immune-
and inflammation. The present study was conducted to evaluate TLR-4 gene polymorphism in patients with CaP. MATERIAL AND METHODS: DNA was isolated from blood samples of 198 patients with CaP, 200 cases of Benign Prostatic Hyperplasia (BPH) and 119 controls. TLR-4 gene polymorphisms Asp299Gly and Thr399Ile were determined by Restriction Fragment Length Polymorphism (RFLP) technique using Nco1 and Hinf 1 restriction enzymes. All statistical calculations were performed using SPSS for windows, version 13 (SPSS Inc., Chicago, Illinois, USA). RESULTS: A significantly high proportion of patients with CaP had AG genotype (16.6%) as compared to control (4.2%) [OR=4.4, 95% CI (1.57-13.26), P =0.0013] with respect to Asp299Gly single nucleotide polymorphism (SNP). AA genotype showed a protective effect towards CaP development [OR=0.39, 95% CI (0.18-0.83), P=0.007). A trend was observed towards development of BPH with respect to AG genotype (P=0.06). Thr399Ile SNP was not significantly different among the population groups studied. CONCLUSIONS: This finding highlights the genetic predispositions to CaP with respect to TLR-4 gene. Individuals with Asp299Gly polymorphism having AG genotype appear to have four fold higher risk for development of Prostate cancer.
time, amount of prostate tissue resected, and blood loss was the same in both
groups (all, p>0.05). The mean duration of follow-up was 9.02 and 8.53 months
in patients receiving TURP and STRUP+TUIBN, respectively. At 6 months
postoperatively, IPSS was 4.26+/−1.22 and 4.18+/−1.47 in patients receiving
TURP and STRUP+TUIBN, respectively (p>0.05), and the Qmax in patients
receiving STRUP+TUIBN was markedly higher than in those receiving TURP
(28.28+/−6.46 mL/s vs. 21.59+/−7.14 mL/s; p<0.05). Bladder neck contracture
and urinary tract infections were observed in 3 and 5 patients receiving TURP,
respectively, and none in STURP. CONCLUSIONS: STRUP+TUIBN may offer a
more effective and safer alternative to TURP for small volume BPH patients.

[1039]
**TITULO / TITLE:** A Gap in Disease-Specific Survival Between Younger and
Older Adults With De Novo Metastatic Renal Cell Carcinoma: Results of a
SEER Database Analysis.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** Clin Genitourin Cancer. 2013 May 3. pii: S1558-

**AUTORES / AUTHORS:** Nelson RA; Vogelzang N; Pal SK

**INSTITUCION / INSTITUTION:** Division of Biostatistics, Department of Information
Science, City of Hope Comprehensive Cancer Center, Duarte, CA.

**RESUMEN / SUMMARY:** BACKGROUND: Consistent with other data sets, our
own institutional series suggests that survival in patients aged >/= 75 years with
metastatic renal cell carcinoma (mRCC) is inferior to that in patients < 75 years.
We sought to confirm these trends through exploration of the Surveillance,
Epidemiology and End Results (SEER) registry. PATIENTS AND METHODS:
We assessed disease-specific survival (DSS) in 6204 patients with clear cell,
papillary, or chromophobe mRCC diagnosed between 1992 and 2009, with the
a priori hypothesis that DSS was shorter in patients aged >/= 75 years.
Analyses were further stratified by the period of diagnosis, either between 1992
and 2004 (the “cytokine era”) or 2005 to 2009 (the “targeted therapy” era).
Univariate and multivariate analyses were conducted to determine the
association between clinicopathologic characteristics and DSS. RESULTS:
DSS was shorter in patients aged >/= 75 years than in patients aged < 75
years (9 vs. 16 months; P < .0001). In patients 18 to 74 years, DSS was
superior in the targeted therapy era compared with the cytokine era (P < .0001).
However, in patients >/= 75 years, no difference in DSS was noted between
these periods (P = .90). On multivariate analysis, age >/= 75 years, female sex,
diagnosis during the cytokine era, node-positive disease, and absence of
cytoreductive nephrectomy were independently associated with DSS.
CONCLUSION: DSS appears to be inferior in older adults with mRCC
(specifically, patients aged >/= 75 years). Furthermore, in contrast to their
younger counterparts, no improvement in DSS was seen in older adults in the transition from the cytokine era to the targeted therapy era.

[1040]

**Título / Title:** Clinical and pathological variables that predict changes in tumour grade after radical prostatectomy in patients with prostate cancer.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary


**Autores / Authors:** Sfoungaristos S; Perimenis P

**Institución / Institution:** Patras University Hospital, Urology Department, Patras, Greece.

**Resumen / Summary:**

**Introducción:** Preoperative Gleason score is crucial, in combination with other preoperative parameters, in selecting the appropriate treatment for patients with clinically localized prostate cancer. The aim of the present study is to determine the clinical and pathological variables that can predict differences in Gleason score between biopsy and radical prostatectomy. **Métodos:** We retrospectively analyzed the medical records of 302 patients who had a radical prostatectomy between January 2005 and September 2010. The association between grade changes and preoperative Gleason score, age, prostate volume, prostate-specific antigen (PSA), PSA density, number of biopsy cores, presence of prostatitis and high-grade prostatic intraepithelial neoplasia was analyzed. We also conducted a secondary analysis of the factors that influence upgrading in patients with preoperative Gleason score $<=$6 (group 1) and downgrading in patients with Gleason score $<=$7 (group 2). **Resultados:** No difference in Gleason score was noted in 44.3% of patients, while a downgrade was noted in 13.7% and upgrade in 42.1%. About 2/3 of patients with a Gleason score of $<=$6 upgraded after radical prostatectomy. PSA density ($p = 0.008$) and prostate volume ($p = 0.032$) were significantly correlated with upgrade. No significant predictors were found for patients with Gleason score $<=$7 who downgraded postoperatively. **Conclusión:** Smaller prostate volume and higher values of PSA density are predictors for upgrade in patients with biopsy Gleason score $<=$6 and this should be considered when deferred treatment modalities are planned.

[1041]

**Título / Title:** Review of the economic evaluations of hormonal therapy for patients with locally advanced prostate cancer.

**Resumen / Summary:** Enlace al Resumen / Link to its Summary


**Enlace al texto completo (gratuito o de pago) 1586/erp.13.12
Androgen deprivation therapy (ADT) is used as first-line therapy for locally advanced or metastatic prostate cancer aiming to reduce testosterone to castrate levels. The authors present an overview of the existing cost-effectiveness studies of ADT in prostate cancer. Cost-effectiveness of ADT was reviewed using a systematic search of the peer-reviewed literature, as well as research abstracts presented at various scientific and industry meetings. Most cost-effectiveness analyses of ADT reported results within the accepted societal threshold of US$50,000 cost/quality-adjusted life year needed to adopt new technology.

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**TÍTULO / TITLE:** Concurrent chemoradiotherapy with low dose weekly gemcitabine in medically inoperable muscle-invasive bladder cancer patients.

**RESUMEN / SUMMARY:** PURPOSE: We aimed to determine the efficacy and the toxicity of low dose weekly gemcitabine with radiation therapy in medically unfit muscle-invasive bladder cancer patients. METHODS: Twenty-six patients were included into the retrospective analysis. Weekly gemcitabine was administered 75 mg/m2 with a median dose of 63 Gy radiation therapy. Clinical target volume was defined as the urinary bladder only in conformal treatment planning. RESULTS: Median follow-up was 51 months (range 14-118 months). Complete response rate was 62.5 %. The 5-year local progression-free survival, disease-specific survival and overall survival rates were 40.6, 59.5 and 58.5 %, respectively. Concurrent chemotherapy was continued in 80.7 % of patients without any interruption. Gemcitabine was stopped due to grade 3 thrombocytopenia (n = 1), cardiac angina (n = 1), chronic obstructive pulmonary disease exacerbation (n = 1) or patients’ reluctance (n = 2). CONCLUSIONS: Low dose weekly gemcitabine with concurrent radiotherapy is a tolerable regimen and have comparable outcomes with platinum-based combined treatments in muscle-invasive bladder cancer. Prospective randomized trials can help in understanding the safety and efficacy of this treatment specially in medically unfit patients.
**TÍTULO / TITLE:** Effects of Serenoa Repens, Selenium and Lycopene (Profluss®) on chronic inflammation associated with Benign Prostatic Hyperplasia: results of “FLOG” (Flogosis and Profluss in Prostatic and Genital Disease), a multicentre Italian study.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Morgia G; Cimino S; Favilla V; Russo GI; Squadrito F; Mucciardi G; Masieri L; Minutoli L; Grosso G; Castelli T

**INSTITUCIÓN / INSTITUTION:** Department of Urology and Department of Hygiene and Public Health, University of Catania, Catania, Department of Urology and Department of Clinical and Experimental Medicine and Pharmacology - Section of Pharmacology, University of Messina Messina and Department of Urology, University of Florence, Florence, Italy.

**RESUMEN / SUMMARY:** Objective: To evaluate the efficacy of Profluss® on prostatic chronic inflammation (PCI). Materials and Methods: We prospectively enrolled 168 subjects affected by LUTS due to bladder outlet obstruction submitted to 12 cores prostatic biopsy for suspected prostate cancer + 2 cores collected for PCI valuation. First group consisted of 108 subjects, with histological diagnosis of PCI associated with BPH and high grade PIN and/or ASAP, randomly assigned to 1:1 ratio to daily Profluss® (group I) for 6 months or to control group (group Ic). Second group consisted of 60 subjects, with histological diagnosis of BPH, randomly assigned to 1:1 ratio to daily Profluss® + a-blockers treatment (group II) for 3 months or to control group (group IIc). After 6 months first group underwent 24 cores prostatic re-biopsy + 2 cores for PCI while after 3 months second group underwent two-cores prostatic for PCI. Specimens were evaluated for changes in inflammation parameters and for density of T-cells (CD3, CD8), B-cells (CD20) and macrophages (CD68).

Results: At follow-up there were statistical significant reductions of extension and grading of flogosis, mean values of CD20, CD3, CD68 and mean PSA value in group I compared to Ic, while extension and grading of flogosis in group II were inferior to IIc but not statistical significant. A statistically significant reduction in the density of CD20, CD3, CD68, CD8 was demonstrated in group II in respect to control IIc. Conclusions: Serenoa repens+Selenium+Lycopene may have an anti-inflammatory activity that could be of interest in the treatment of PCI in BPH and/or PIN/ASAP patients.

**TÍTULO / TITLE:** Analysis of the correlation between endorectal MRI response to neoadjuvant chemotherapy and biochemical recurrence in patients with high-risk localized prostate cancer.

[1044]
RESUMEN / SUMMARY:  Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 1038/pcan.2013.15

AUTORES / AUTHORS:  Galsky MD; Xie W; Nakabayashi M; Ross RW; Fennessy FM; Tempany CM; Choueiri TK; Khine K; Kantoff PW; Taplin ME; Oh WK

INSTITUCIÓN / INSTITUTION:  Department of Medicine, Mount Sinai School of Medicine, Tisch Cancer Institute, New York, NY, USA.

RESUMEN / SUMMARY:  Background: Intermediate end points are desirable to expedite the integration of neoadjuvant systemic therapy into the treatment strategy for high-risk localized prostate cancer. Endorectal magnetic resonance imaging at 1.5 Tesla (1.5T erMRI) response has been utilized as an end point in neoadjuvant trials but has not been correlated with clinical outcomes.

Methods: Data were pooled from two trials exploring neoadjuvant chemotherapy in high-risk localized prostate cancer. Trial 1 explored docetaxel for 6 months and Trial 2 explored docetaxel plus bevacizumab for 4.5 months, both before radical prostatectomy. erMRI was done at baseline and end of chemotherapy. 1.5T erMRI response, based upon T2W sequences, was recorded. Multivariable Cox regression was undertaken to evaluate the association between clinical parameters and biochemical recurrence.

Results: There were 53 evaluable patients in the combined analysis: 20 (33%) achieved a PSA response, 16 (27%) achieved an erMRI partial response and 24 (40%) achieved an erMRI minor response. Median follow-up was 4.2 years, and 33 of 53 evaluable (62%) patients developed biochemical recurrence. On multivariable analysis, PSA response did not correlate with biochemical recurrence (hazard ratio=0.58, 95% confidence interval (CI) 0.25-1.33) and paradoxically erMRI response was associated with a significantly shorter time to biochemical recurrence (hazard ratio=2.47, 95% CI 1.00-6.13).

Conclusions: Response by 1.5T erMRI does not correlate with a decreased likelihood of biochemical recurrence in patients with high-risk localized prostate cancer treated with neoadjuvant docetaxel and may be associated with inferior outcomes. These data do not support the use of 1.5T erMRI response as a primary end point in neoadjuvant chemotherapy trials.

Prostate Cancer and Prostatic Disease advance online publication, 28 May 2013; doi:10.1038/pcan.2013.15.

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[1045]

TÍTULO / TITLE:  Can 80 W KTP Laser Vaporization Effectively Relieve the Obstruction in Benign Prostatic Hyperplasia?: A Nonrandomized Trial.

RESUMEN / SUMMARY:  Enlace al Resumen / Link to its Summary

PURPOSE: There is little data evaluating the changes of severity of bladder outlet obstruction after 80 W potassium-titanyl-phosphate (KTP) photoselective laser vaporization prostatectomy (PVP) by pressure-flow study. We evaluated the efficacy of PVP to relieve the obstruction in benign prostate hyperplasia (BPH) compared with transurethral resection of the prostate (TURP). MATERIALS AND METHODS: This is a prospective, non-randomized single center study. The inclusion criteria were as follows: Men suffering from lower urinary tract symptoms (LUTS) secondary to BPH, age >/=50 years, International Prostatic Symptom Score (IPSS) >/=13, maximum flow rate (Qmax) </=15 ml/s, and ability to give fully informed consent. Patients with neurogenic cause or detrusor underactivity were excluded. The IPSS, bother score, Qmax, postvoid residual volume (PVR), detrusor pressure at maximum flow rate (PdetQmax), bladder outlet obstruction index (BOOI), and prostate volume were measured before and 6 months after surgery and compared between PVP and TURP. RESULTS: Sixty-seven patients (53 in PVP, 14 in TURP) were evaluable. In both groups, the IPSS, bother score, Qmax, and PVR had significantly improved (p<0.05), and there were no differences between the changes in those parameters. PVP could effectively reduce the PdetQmax, prostate volume, and BOOI from baseline (from 68.7+/-23.3 to 40.6+/-11.2 cmH2O, 49.5+/-16.3 to 31.3+/-12.1 ml, 49.8+/-25.6 to 9.8+/-20.7), similar to TURP. There were no differences in postoperative PdetQmax, prostate volume, or BOOI between the two groups. The percentage of patients with BOOI >/=40 was decreased from 64% to 4% in the PVP group and from 86% to 14% in the TURP group. CONCLUSIONS: PVP could reduce the prostate volume effectively and relieve bladder outlet obstruction similar to TURP by the 6-month follow up in men with BPH.

[1046]
TÍTULO / TITLE: - Five-year clinical effects of donor bone marrow cells infusions in kidney allograft recipients: improved graft function and higher graft survival.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Chimerism. 2013 May 2;4(3).
AUTORES / AUTHORS: - Solgi G; Gadi V; Paul B; Mytilineos J; Pourmand G; Mehrsai A; Ranjbar M; Mohammadnia M; Nikbin B; Amirzargar AA
INSTITUCIÓN / INSTITUTION: - Immunology Department; School of Medicine; Hamadan University of Medical Sciences; Hamadan, Iran.
RESUMEN / SUMMARY: - Augmentation of microchimerism in solid organ transplant recipients by donor bone marrow cells (DBMC) infusion may promote
immune hyporesponsiveness and consequently improve long-term allograft survival. Between March 2005 and July 2007, outcomes for 20 living unrelated donor (LURD) primary kidney recipients with concurrent DBMC infusion (an average of 2.19 +/- 1.13 x 10^9 donor cells consisting of 2.66 +/- 1.70 x 10^7 CD34 (+) cells) were prospectively compared with 20 non-infused control allograft recipients given similar conventional immunosuppressive regimens. With five years of clinical follow up, a total of 11 cases experienced rejection episodes (3 DBMI patients vs. 8 controls, p = 0.15). One DBMC-infused patient experienced chronic rejection vs. two episodes (1 biopsy-confirmed) in the control patients. Actuarial and death-censored 5-y graft survival was significantly higher in infused patients compared with controls (p = 0.01 and p = 0.03, respectively). Long-term graft survival was significantly associated with pre-transplant anti-HLA antibodies (p = 0.01), slightly with peripheral microchimerism (p = 0.09) and CD4 (+) CD25 (+) FoxP3 (+) T cells (p = 0.09). Immunosuppressant dosing was lower in infused patients than controls, particularly for mycophenolate mofetil (p = 0.001). The current findings as well as our previous reports on these patients indicates clinical improvement in long-term graft survival of renal transplant patients resulting from low-dose DBMC infusion given without induction therapy.

[1047]

TÍTULO / TITLE: - Predicting factors for stent failure-free survival in patients with a malignant ureteral obstruction managed with ureteral stents.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Yu SH; Ryu JG; Jeong SH; Hwang EC; Jang WS; Hwang IS; Yu HS; Kim SO; Jung SI; Kang TW; Kwon DD; Park K; Hwang JE; Kim GS

INSTITUCIÓN / INSTITUTION: - Department of Urology, Chonnam National University Medical School, Gwangju, Korea.

RESUMEN / SUMMARY: - PURPOSE: To determine predictive factors for stent failure-free survival in patients treated with a retrograde ureteral stent for a malignant ureteral obstruction. MATERIALS AND METHODS: We retrospectively reviewed 71 patients who underwent insertion of a cystoscopic ureteral stent due to a malignant ureteral obstruction between May 2004 and June 2011. Performance status, type of cancer, hydronephrosis grade, location of the obstruction, presence of bladder invasion, C-reactive protein (CRP), serum albumin, and inflammation-based prognostic score (Glasgow prognostic score, GPS) were assessed using a Cox proportional regression hazard model as predicting factors for stent failure. RESULTS: A univariate analysis indicted that hypoalbuminemia (<3.5 g/dL; hazard ratio [HR], 2.43; 95% confidence
interval [CI], 1.21 to 4.86; p=0.012), elevated CRP (≥1 mg/dL; HR, 4.79; 95% CI, 2.0 to 11.1; p=0.001), and presence of a distal ureter obstruction (HR, 3.27; 95% CI, 1.19 to 8.95; p=0.021) were associated with stent failure-free survival. A multivariate analysis revealed that the presence of a mid and lower ureteral obstruction (HR, 3.27; 95% CI, 1.19 to 8.95; p=0.007), GPS ≥1 (HR, 7.22; 95% CI, 2.89 to 18.0; p=0.001), and elevated serum creatinine before ureteral stent placement (≥1.2 mg/dL; HR, 2.16; 95% CI, 1.02 to 4.57; p=0.044) were associated with stent failure-free survival. CONCLUSIONS: A mid or lower ureteral obstruction, GPS ≥1, and serum creatinine before ureteral stent insertion >1.2 mg/dL were unfavorable predictors of stent failure-free survival. These factors may help urologists predict survival time.

[1048]

TÍTULO / TITLE: Bcl-2 Overexpression Inhibits Generation of Intracellular Reactive Oxygen Species and Blocks Adriamycin-induced Apoptosis in Bladder Cancer Cells.

RESUMEN / SUMMARY: Resistance to induction of apoptosis is a major obstacle for bladder cancer treatment. Bcl-2 is thought to be involved in anti-apoptotic signaling. In this study, we investigated the effect of Bcl-2 overexpression on apoptotic resistance and intracellular reactive oxygen species (ROS) generation in bladder cancer cells. A stable Bcl-2 overexpression cell line, BIU87-Bcl-2, was constructed from human bladder cancer cell line BIU87 by transfecting recombinant Bcl-2 [pcDNA3.1(+)-Bcl-2]. The sensitivity of transfected cells to adriamycin (ADR) was assessed by MTT assay. Apoptosis was examined by flow cytometry and acidine orange fluorescence staining. Intracellular ROS was determined using flow cytometry, and the activities of superoxide dismutase (SOD) and catalase (CAT) were also investigated by the xanthinoxidase and visible radiation methods using SOD and CAT detection kits. The susceptibility of BIU87-Bcl-2 cells to ADR treatment was significantly decreased as compared with control BIU87 cells. Enhanced expression of Bcl-2 inhibited intracellular ROS generation following ADR treatment. Moreover, the suppression of SOD and CAT activity induced by ADR treatment was blocked in the BIU87-Bcl-2 case but not in their parental cells. The overexpression of Bcl-2 renders human bladder cancer cells resistant to ADR-induced apoptosis and ROS might act as an important secondary messenger in this process.

[1049]
TÍTULO / TITLE: - Kidney cancer: AXIS trial data confirm axitinib as second-line option for mRCC.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.100
AUTORES / AUTHORS: - Payton S

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1111/jocn.12178
AUTORES / AUTHORS: - Hsiao CP; Moore IM; Insel KC; Merkle CJ
INSTITUCIÓN / INSTITUTION: - National Institute of Nursing Research, National Institutes of Health, Bethesda, MD, USA.
RESUMEN / SUMMARY: - AIMS AND OBJECTIVES: To explore the association between symptoms, symptom distress and symptom self-management and to identify effective strategies of symptom self-management in men with non-metastatic prostate cancer following radical prostatectomy or radiation therapy.
BACKGROUND: Men receiving treatments for localised prostate cancer experience symptoms of urinary incontinence, urinary obstruction/irritation, bowel difficulties and sexual dysfunction. Understanding patients' symptom experiences and identifying strategies that they use to manage these symptoms are imperative for symptom management planning.
DESIGN: A descriptive, cross-sectional study was conducted with a sample of 53 men, who were within three months of the initiation of their treatment.
METHODS: The Symptom Indexes and the Strategy and Effectiveness of Symptom Self-Management questionnaires were used to measure symptoms, symptom distress and symptom self-management. Descriptive statistics, t-tests, correlations and multiple regressions were used to analyse the data.
RESULTS: Symptoms were significantly correlated with symptom-related distress ($r = 0.67$, $p < 0.01$). Frequency of symptoms was significantly associated with symptom self-management strategies for urinary (beta = 0.50, $p < 0.01$), bowel (beta = 0.71, $p < 0.01$) and sexual problems (beta = 0.28, p = 0.05). The most effective strategies were as follows: pads and doing Kegel exercise for managing urinary problems, rest and endurance for bowel symptoms, and expressing feelings and finding alternative ways to express affection for management of sexual dysfunction.
CONCLUSIONS: Assessing symptom self-management among men with newly diagnosed prostate cancer can help healthcare providers develop strategies that will enhance health-related quality of life.
RELEVANCE TO CLINICAL PRACTICE: Results provide information on effective strategies that patients with prostate cancer found to reduce their symptoms. The
strategies used provide a foundation for developing and testing interventions for personalised symptom management.

[1051]
TÍTULO / TITLE: - Transcatheter arterial chemotherapy with miriplatin for hepatocellular carcinoma patients with chronic renal failure: report of three cases.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Imai N; Ikeda K; Seko Y; Kawamura Y; Sezaki H; Hosaka T; Akuta N; Kobayashi M; Saitoh S; Suzuki F; Suzuki Y; Arase Y; Kumada H
INSTITUCIÓN / INSTITUTION: - Department of Hepatology, Toranomon Hospital, Tokyo, Japan.
RESUMEN / SUMMARY: - Miriplatin is a novel lipophilic platinum complex that was developed to treat hepatocellular carcinoma (HCC). Although HCC patients frequently have coexisting chronic renal failure, little prospective data are available regarding the clinical toxicity of chemotherapeutic agents used to treat HCC patients with chronic renal failure. In a phase II study, the plasma concentration of total platinum in patients who received miriplatin was very low, and no severe renal toxicity caused by miriplatin injection was reported. Here, we present three cases of HCC with stage 4 chronic renal failure who received transcatheter arterial chemotherapy with miriplatin. All cases were male, ages 72, 84, and 83 years, and had serum creatinine levels of 2.3, 1.6, and 1.9 mg/dL, respectively. Their estimated glomerular filtration rates were 21.9, 20.3, and 22.2 mL/min, respectively. All cases were treated for unresectable HCC with transcatheter arterial chemotherapy with miriplatin. No serious adverse events were observed, and serum creatinine levels did not elevate, even in the patient who experienced renal failure caused by cisplatin administration. These results might suggest that transcatheter arterial chemotherapy with miriplatin can be safely used in HCC patients with chronic renal failure.

[1052]
TÍTULO / TITLE: - Feasibility and radiation induced toxicity regarding the first application of transperineal implementation of biocompatible balloon for high dose radiotherapy in patients with prostate carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Imai N; Ikeda K; Seko Y; Kawamura Y; Sezaki H; Hosaka T; Akuta N; Kobayashi M; Saitoh S; Suzuki F; Suzuki Y; Arase Y; Kumada H
INSTITUCIÓN / INSTITUTION: - Department of Hepatology, Toranomon Hospital, Tokyo, Japan.
OBJECTIVE: To evaluate the feasibility of the transperineal implementation of biocompatible balloon (Prospace) and the acute toxicity of high dose 3DCRT in patients with localized low risk prostate cancer.

Materials and methods: Between December 2011 and April 2012, fifteen patients were treated with external 3DCRT consisted of 76--78 Gy in 38--39 daily fractions (2.0 Gy/fraction). Before 3DCRT, we placed the Prospace through the perineum by a minimally invasive procedure in the intermediate space between the rectum and the prostate. The primary study endpoint was the evaluation of acute toxicity according to the EORTC/RTOG radiation toxicity scale. Erectile function was evaluated with the IIEF-5 questionnaire. Rectosigmoidoscopy was performed at baseline, at the end of 3DCRT and 3 months thereafter in order to assess also the rectal toxicity according to Subjective-RectoSigmoid (S-RS) scale. The evaluation of pain related to Prospace implementation was done with the visual analogue score (VAS).

RESULTS: The acute toxicities were as follows: grade I GI toxicity in two patients and for GU toxicity, three patients with grade I of nocturia, four patients with grade I of frequency, two patients with grade I and two patients with grade II of dysouria. The mean score of rectal toxicity according to S-RS score was 1.8(+/-0.6). The mean VAS score related to Prospace was 1.4(+/-0.5). Erectile function was unchanged. The Prospace device was found stable in sequential CTs during irradiation.

CONCLUSIONS: The implementation of PROSPACE was feasible, while the acute radiation toxicity was low and comparable with IMRT techniques.
native kidney after renal transplantation. RESULTS: The patients included three males and two females with a mean age of 63 years (range, 52 to 74). The incidence of RCC was 0.35%. The median interval between renal transplantation and RCC occurrence was 16.2 years (range, 9 to 20). All of our patients with RCC had developed renal cysts either before (n = 3) or after (n = 2) renal transplantation. The mean duration of dialysis was 12 months (range, 2 to 39). Of the five patients, four underwent dialysis treatment for less than 8 months. All the RCCs were low grade at the time of diagnosis. Four patients underwent radical nephrectomy, and one patient refused the operation. The four patients who underwent radical nephrectomy showed no evidence of local recurrence or distant metastasis during the median follow-up of 2.9 years. However, the patient who did not undergo surgery developed spinal metastasis from the RCC 6 years later. CONCLUSIONS: This study suggests that the follow-up period is an important factor for the development of RCC in renal transplant recipients, and more vigorous screening with a longer follow-up period is required in renal transplant recipients.

[1054]
TÍTULO / TITLE: - Preoperative Neutrophil-Lymphocyte Ratio as an Independent Prognostic Marker for Patients With Upper Urinary Tract Urothelial Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Azuma T; Matayoshi Y; Odani K; Sato Y; Sato Y; Nagase Y; Oshi M
INSTITUCIÓN / INSTITUTION: - Department of Urology, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan. Electronic address: tazuma-tky@umin.ac.jp.
RESUMEN / SUMMARY: - BACKGROUND: To predict the prognosis, we evaluated the significance of the preoperative neutrophil-lymphocyte ratio (NLR) in patients with upper urinary tract urothelial carcinoma (UUTUC). PATIENTS AND METHODS: A cohort of 137 patients diagnosed with UUTUC from 1994 to 2008 at Tokyo Metropolitan Tama Medical Center was enrolled in this retrospective study. Log-rank test and Cox proportional hazards regression models were used for univariate and multivariate analyses. RESULTS: On univariate analysis, pathologic T stage, grade, lymphovascular invasion, C-reactive protein (CRP) level, and NLR were significantly associated with recurrence-free survival (RFS) and cancer-specific survival (CSS). The RFS rates for an NLR < 2.5 and for one >/= 2.5 at 5 years were 74.3% and 30.4%, respectively. The CSS rates for an NLR < 2.5 and for one >/= 2.5 at 5 years were 81.3% and 29.4%, respectively. The multivariate Cox proportional hazards regression models showed that the NLR could be an independent predictor for
RFS and CSS. Based on the results of multivariate analysis, the scoring model was developed. RFS and CSS rates at 5 years were as follows: 0 risk factor, 97.1% and 97.0%, respectively; 1 risk factor, 91.1% and 90.9%, respectively; 2 risk factors, 39.5% and 58.6%, respectively; 3 risk factors, 26.6% and 28.6%, respectively; and 4 risk factors, 6.0% and 5.6%, respectively. CONCLUSIONS: The preoperative NLR is an independent prognostic predictor. The model based on the NLR and pathologic factors can be useful in clinical practice.

[1055]

TÍTULO / TITLE: - Sociodemographic and health-related predictors of self-reported mammogram, faecal occult blood test and prostate specific antigen test use in a large Australian study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Weber MF; Cunich M; Smith DP; Salkeld G; Sitas F; O'Connell D
INSTITUCIÓN / INSTITUTION: - Cancer Research Division, Cancer Council NSW, PO Box 572, Kings Cross, Sydney, NSW 1340, Australia. mariannew@nswcc.org.au.
RESUMEN / SUMMARY: - BACKGROUND: While several studies have examined factors that influence the use of breast screening mammography, faecal occult blood tests (FOBT) for bowel cancer screening and prostate specific antigen (PSA) tests for prostate disease in Australia, research directly comparing the use of these tests is sparse. We examined sociodemographic and health-related factors associated with the use of these tests in the previous two years either alone or in combination. METHODS: Cross-sectional analysis of self-reported questionnaire data from 96,711 women and 82,648 men aged 50 or over in The 45 and Up Study in NSW (2006-2010). RESULTS: 5.9% of men had a FOBT alone, 44.9% had a PSA test alone, 18.7% had both tests, and 30.6% had neither test. 3.2% of women had a FOBT alone, 56.0% had a mammogram alone, 16.2% had both and 24.7% had neither test. Among men, age and socioeconomic factors were largely associated with having both FOBT and PSA tests. PSA testing alone was largely associated with age, family history of prostate cancer, health insurance status and visiting a doctor. Among women, age, use of hormone replacement therapy (HRT), health insurance status, family history of breast cancer, being retired and not having a disability were associated with both FOBT and mammograms. Mammography use alone was largely associated with age, use of HRT and family history of breast cancer. FOBT use alone among men was associated with high income, living in regional areas and being fully-retired and among women, being fully-retired or sick/disabled. CONCLUSIONS: These results add to the literature on
sociodemographic discrepancies related to cancer screening uptake and highlight the fact that many people are being screened for one cancer when they could be screened for two.

[1056]
TÍTULO / TITLE: - Impaired Kidney Function at Hospital Discharge and Long-Term Renal and Overall Survival in Patients Who Received CRRT.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Stads S; Fortrie G; van Bommel J; Zietse R; Betjes MG
INSTITUCIÓN / INSTITUTION: - Department of Nephrology and Transplantation and, daggerDepartment of Intensive Care, Erasmus Medical Center, Rotterdam, The Netherlands.
RESUMEN / SUMMARY: - BACKGROUND AND OBJECTIVES: Critically ill patients with AKI necessitating renal replacement therapy (RRT) have high in-hospital mortality, and survivors are at risk for kidney dysfunction at hospital discharge. The objective was to evaluate the association between impaired kidney function at hospital discharge with long-term renal and overall survival.
DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS: Degree of kidney dysfunction in relation to long-term effects on renal survival and patient mortality was investigated in a retrospective cohort study of 1220 adults admitted to an intensive care unit who received continuous RRT between 1994 and 2010.
RESULTS: After hospital discharge, median follow-up of survivors (n=475) was 8.5 years (range, 1-17 years); overall mortality rate was 75%. Only 170 (35%) patients were discharged with an estimated GFR (eGFR) >60 ml/min per 1.73 m2. Multivariate proportional hazards regression analysis demonstrated that age, nonsurgical type of admission, preexisting kidney disease, malignancy, and eGFR of 29-15 ml/min per 1.73 m2 (hazard ratio [HR], 1.62; 95% confidence interval [CI], 1.01 to 2.58) and eGFR <15 ml/min per 1.73 m2 (HR, 1.93; 95% CI, 1.23 to 3.02) at discharge were independent predictors of increased mortality. Renal survival was significantly associated with degree of kidney dysfunction at discharge. An eGFR of 29-15 ml/min per 1.73 m2 (HR, 26.26; 95% CI, 5.59 to 123.40) and <15 ml/min per 1.73 m2 (HR, 172.28; 95% CI, 37.72 to 786.75) were independent risk factors for initiation of long-term RRT.
CONCLUSIONS: Most critically ill patients surviving AKI necessitating RRT have impaired kidney function at hospital discharge. An eGFR <30 ml/min per 1.73 m2 is a strong risk factor for decreased long-term survival and poor renal survival.

[1057]
High CRP values predict poor survival in patients with penile cancer.

Background: High levels of circulating C-reactive protein (CRP) have recently been linked to poor clinical outcome in various malignancies. The aim of this study was to evaluate the prognostic significance of the preoperative serum CRP level in patients with squamous cell carcinoma (SCC) of the penis.

Methods: This retrospective analysis included 79 penile cancer patients with information about their serum CRP value prior to surgery who underwent either radical or partial penectomy at two German high-volume centers (Ulm University Medical Center and Hannover Medical School) between 1990 and 2010. They had a median (mean) follow-up of 23 (32) months.

Results: A significantly elevated CRP level (>15 vs. \(\leq 15\) mg/l) was found more often in patients with an advanced tumor stage (\(\geq pT2\)) (38.9 vs. 11.6%, \(p=0.007\)) and in those with nodal disease at diagnosis (50.0 vs. 14.6%, \(p=0.007\)). However, high CRP levels were not associated with tumor differentiation (\(p=0.53\)). The Kaplan-Meier 5-year cancer-specific survival (CSS) rate was 38.9% for patients with preoperative CRP levels above 15 mg/l and 84.3% for those with lower levels (\(p=0.001\)). Applying multivariate analysis and focusing on the subgroup of patients without metastasis at the time of penile surgery, both advanced local tumor stage (>\(pT2\); HR 8.8, \(p=0.041\)) and an elevated CRP value (>15 mg/l; HR 3.3, \(p=0.043\)) were identified as independent predictors of poor clinical outcome in patients with penile cancer.

Conclusions: A high preoperative serum CRP level was associated with poor survival in patients with penile cancer. If larger patient populations confirm its prognostic value, its routine use could enable better risk stratification and risk-adjusted follow-up of patients with SCC of the penis.

The role of sarcosine metabolism in prostate cancer progression.

Background: Sarcosine, a choline-derived substrate, has recently been suggested as a potential biomarker for prostate cancer. Some studies have reported that sarcosine metabolism is associated with prostate cancer progression.

Methods: We performed a systematic review and meta-analysis of published studies to evaluate the association between sarcosine metabolism and prostate cancer progression.

Results: A total of 12 studies were included in the meta-analysis. The pooled odds ratio (OR) for the association between sarcosine metabolism and prostate cancer progression was 1.50 (95% CI: 1.26-1.78, \(p<0.001\)). The heterogeneity across studies was low (\(I^2=21\%\)).

Conclusions: Sarcosine metabolism is associated with prostate cancer progression. Further research is needed to confirm these findings and to explore the potential clinical implications of these results.
Metabolomic profiling of prostate cancer (PCa) progression identified markedly elevated levels of sarcosine (N-methyl glycine) in metastatic PCa and modest but significant elevation of the metabolite in PCa urine. Here, we examine the role of key enzymes associated with sarcosine metabolism in PCa progression. Consistent with our earlier report, sarcosine levels were significantly elevated in PCa urine sediments compared to controls, with a modest area under the receiver operating characteristic curve of 0.71. In addition, the expression of sarcosine biosynthetic enzyme, glycine N-methyltransferase (GNMT), was elevated in PCa tissues, while sarcosine dehydrogenase (SARDH) and pipecolic acid oxidase (PIPOX), which metabolize sarcosine, were reduced in prostate tumors. Consistent with this, GNMT promoted the oncogenic potential of prostate cells by facilitating sarcosine production, while SARDH and PIPOX reduced the oncogenic potential of prostate cells by metabolizing sarcosine. Accordingly, addition of sarcosine, but not glycine or alanine, induced invasion and intravasation in an in vivo PCa model. In contrast, GNMT knockdown or SARDH overexpression in PCa xenografts inhibited tumor growth. Taken together, these studies substantiate the role of sarcosine in PCa progression.
hypermethylation (13%). Several of the most significantly altered loci (CAV1, EVX1, MCF2L, and FGF1) were then used as probes to map the extent of these DNA methylation changes in normal tissues from prostates containing cancer. In TA tissues, the extent of methylation was similar both adjacent (2 mm) and at a distance (>1 cm) from tumor foci. These loci were also able to distinguish NTA from TA tissues in a validation set of patient samples. These mapping studies indicate that a spatially widespread epigenetic defect occurs in the peripheral prostate tissues of men who have PCa that may be useful in the detection of this disease.

[1060]

**TITULO / TITLE:** - Epigenomic alterations in localized and advanced prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Lin PC; Giannopoulou EG; Park K; Mosquera JM; Sboner A; Tewari AK; Garraway LA; Beltran H; Rubin MA; Elemento O

**INSTITUCIÓN / INSTITUTION:** - Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, NY 10065, USA.

**RESUMEN / SUMMARY:** - Although prostate cancer (PCa) is the second leading cause of cancer death among men worldwide, not all men diagnosed with PCa will die from the disease. A critical challenge, therefore, is to distinguish indolent PCa from more advanced forms to guide appropriate treatment decisions. We used Enhanced Reduced Representation Bisulfite Sequencing, a genome-wide high-coverage single-base resolution DNA methylation method to profile seven localized PCa samples, seven matched benign prostate tissues, and six aggressive castration-resistant prostate cancer (CRPC) samples. We integrated these data with RNA-seq and whole-genome DNA-seq data to comprehensively characterize the PCa methylome, detect changes associated with disease progression, and identify novel candidate prognostic biomarkers. Our analyses revealed the correlation of cytosine guanine dinucleotide island (CGI)-specific hypermethylation with disease severity and association of certain breakpoints (deletion, tandem duplications, and interchromosomal translocations) with DNA methylation. Furthermore, integrative analysis of methylation and single-nucleotide polymorphisms (SNPs) uncovered widespread allele-specific methylation (ASM) for the first time in PCa. We found that most DNA methylation changes occurred in the context of ASM, suggesting that variations in tumor epigenetic landscape of individuals are partly mediated by genetic differences, which may affect PCa disease progression. We further selected a panel of 13 CGIs demonstrating increased DNA methylation with disease progression and validated this panel in an independent cohort of 20 benign prostate tissues, 16 PCa, and 8 aggressive CRPCs. These results warrant
clinical evaluation in larger cohorts to help distinguish indolent PCa from advanced disease.

[1061]
**TÍTULO / TITLE:** The authors reply: renal cell carcinoma in kidney transplant recipients and dialysis patients.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Lee HH; Han WK

**INSTITUCIÓN / INSTITUTION:** Department of Urology, Urologic Science Institute, Yonsei University College of Medicine, Seoul, Korea.

[1062]
**TÍTULO / TITLE:** Advances in the management of muscle-invasive bladder cancer through risk prediction, risk communication, and novel treatment approaches.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Galsky MD; Domingo-Domenech J

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**RESUMEN / SUMMARY:** Although level I evidence supports the use of neoadjuvant cisplatin-based chemotherapy followed by radical cystectomy for the management of patients with muscle-invasive bladder cancer (MIBC), these treatment modalities are utilized in only a subset of patients. The reasons for lack of implementation of these treatment standards are multiple; patients may be considered ineligible for cisplatin or too old for safe cystectomy. Better means of determining a patient’s probability of recurrence with surgery alone, or likelihood of benefit with neoadjuvant chemotherapy, are clearly needed. Models have been developed to individualize estimates of non-organ-confined disease based on pretreatment variables. It is critical that clinicians are able to effectively communicate complex risk-related data to patients to facilitate a shared medical decision.

[1063]
**TÍTULO / TITLE:** High dose rate brachytherapy as monotherapy for localised prostate cancer: a hypofractionated two-implant approach in 351 consecutive patients.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Tselis N; Tunn UW; Chatzikonstantinou G; Milickovic N; Baltas D; Ratka M; Zamboglou N

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Klinikum Offenbach, Starkenburgring 66, 63069 Offenbach, Germany. ntselis@hotmail.com.

RESUMEN / SUMMARY: - BACKGROUND: To report the clinical outcome of high dose rate brachytherapy as sole treatment for clinically localised prostate cancer. METHODS: Between March 2004 and January 2008, a total of 351 consecutive patients with clinically localised prostate cancer were treated with transrectal ultrasound guided high dose rate brachytherapy. The prescribed dose was 38.0 Gy in four fractions (two implants of two fractions each of 9.5 Gy with an interval of 14 days between the implants) delivered to an intraoperative transrectal ultrasound real-time defined planning treatment volume. Biochemical failure was defined according to the Phoenix Consensus and toxicity evaluated using the Common Toxicity Criteria for Adverse Events version 3. RESULTS: The median follow-up time was 59.3 months. The 36 and 60 month biochemical control and metastasis-free survival rates were respectively 98%, 94% and 99%, 98%. Toxicity was scored per event with 4.8% acute Grade 3 genitourinary and no acute Grade 3 gastrointestinal toxicity. Late Grade 3 genitourinary and gastrointestinal toxicity were respectively 3.4% and 1.4%. No instances of Grade 4 or greater acute or late adverse events were reported. CONCLUSIONS: Our results confirm high dose rate brachytherapy as safe and effective monotherapy for clinically organ-confined prostate cancer.

[1064]

TÍTULO / TITLE: - A248, a novel synthetic HDAC inhibitor, induces apoptosis through the inhibition of specificity protein 1 and its downstream proteins in human prostate cancer cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Choi ES; Han G; Park SK; Lee K; Kim HJ; Cho SD; Kim HM

INSTITUCIÓN / INSTITUTION: - Department of Oral Pathology, School of Dentistry and Institute of Oral Bioscience, Brain Korea 21 Project, Chonbuk National University, Jeonju 561-756, Republic of Korea.

RESUMEN / SUMMARY: - Histone deacetylase (HDAC) inhibitors are emerging as potent anticancer agents due to their ability to induce apoptosis in various cancer cells, including prostate cancer cells. In the present study, we
synthesized a novel HDAC inhibitor, A248, and investigated its apoptotic activity and molecular target in the DU145 and PC3 human prostate cancer cell lines. A248 inhibited the growth of DU145 and PC3 cells and induced apoptosis, as demonstrated by nuclear fragmentation and the accumulation of cells at subG1 phase of cell cycle. The treatment of DU145 and PC3 prostate cancer cells with A248 resulted in the downregulation of specificity protein 1 (Sp1) expression. Since the expression levels of survivin and Mcl-1 depend on Sp1, we also investigated the effects of A248 on survivin and Mcl-1 expression using western blot analysis and immunocytochemistry. The results showed that A248 markedly decreased the expression of survivin and Mcl-1. These data suggest that A248 has apoptotic activity in human prostate cancer cells and that Sp1 may be the molecular target of A248 treatment for inducing apoptosis in prostate cancer cells.

[1065]
TÍTULO / TITLE: - Small renal masses: Support for active surveillance in patients aged >/=75 years.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Payton S

[1066]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Chang JS; Yoon HI; Cha HJ; Chung Y; Cho Y; Keum KC; Koom WS
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Yonsei University College of Medicine, Seoul, Korea.
contouró la pared interna del uréter mostrada en la CT y calculó su volumen. RESULTADOS: Antes de la simulación, el volumen medido usando la CT de simulación y el escáner de ultrasonido de vejiga fue de 427 mL (rango, 74 a 1,172 mL) y 417 mL (rango, 147 a 1,245 mL), respectivamente.存 strong linear correlation (R = 0.93, p < 0.001) entre los dos resultados. Durante el curso de la terapia, hubo variaciones amplias en el volumen vesical y cada vez, las mediciones fueron inferiores al límite basado con significancia estadística (12/16). A las 6 semanas después de la RT, el volumen medido fue reducido en 59.3% a 175 mL. Comparado con el límite inicial, el volumen vesical fue reducido en promedio 38% o 161 mL cada semana durante 6 semanas.

CONCLUSIÓN: A nuestro conocimiento, este estudio es el primero en demostrar que hay variaciones en el volumen vesical y una reducción en el volumen vesical en pacientes con cáncer rectal. Además, nuestros resultados servirán como base para la implementación de entrenamiento vesical a pacientes que reciben RT con vejiga llena.

[1067]
TÍTULO / TITLE: - Effect of different breathing patterns in the same patient on stereotactic ablative body radiotherapy dosimetry for primary renal cell carcinoma: A case study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Pham D; Kron T; Foroudi F; Siva S
INSTITUCIÓN / INSTITUTION: - Radiotherapy Services, Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia. Electronic address: Daniel.Pham@petermac.org.
RESUMEN / SUMMARY: - Stereotactic ablative body radiotherapy (SABR) for primary renal cell carcinoma (RCC) targets requires motion management strategies to verify dose delivery. This case study highlights the effect of a change in patient breathing amplitude on the dosimetry to organs at risk and target structures. A 73-year-old male patient was planned for receiving 26Gy of radiation in 1 fraction of SABR for a left primary RCC. The patient was simulated with four-dimensional computed tomography (4DCT) and the tumor internal target volume (ITV) was delineated using the 4DCT maximum intensity projection. However, the initially planned treatment was abandoned at the radiation oncologist’s discretion after pretreatment cone-beam CT (CBCT) motion verification identified a greater than 50% reduction in superior to inferior diaphragm motion as compared with the planning 4DCT. This patient was resimulated with respiratory coaching instructions. To assess the effect of the change in breathing on the dosimetry to the target, each plan was recalculated on the data set representing the change in breathing condition. A change from
smaller to larger breathing showed a 46% loss in planning target volume (PTV) coverage, whereas a change from larger breathing to smaller breathing resulted in an 8% decrease in PTV coverage. ITV coverage was similarly reduced by 8% in both scenarios. This case study highlights the importance of tools to verify breathing motion prior to treatment delivery. 4D image guided radiation therapy verification strategies should focus on not only verifying ITV margin coverage but also the effect on the surrounding organs at risk.

[1068]
TÍTULO / TITLE: - The Use of n-Butyl-2 Cyanoacrylate as an Embolic Agent in the Minimally Invasive Treatment of Renal Arteriovenous Malformations.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Poh PG; Tan BS; Tham SC; Tay KH; Htoo AM; Lin MB; Cheng CW; Chong TW; Foo KT; Lim WE
INSTITUCIÓN / INSTITUTION: - University of Glasgow.

[1069]
TÍTULO / TITLE: - The Impact of Gender on Outcomes in Patients With Metastatic Urothelial Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Haines L; Bamias A; Krege S; Lin CC; Hahn N; Ecke TH; Moshier E; Sonpavde G; Godbold J; Oh WK; Galsky MD
INSTITUCIÓN / INSTITUTION: - The Tisch Cancer Institute, Mount Sinai School of Medicine, New York, NY.
RESUMEN / SUMMARY: - BACKGROUND: Although urothelial cancer is more common in men, women with urothelial cancer have inferior survival outcomes. The potential existence of gender-related disparities in patients with metastatic urothelial cancer has not been extensively explored. PATIENTS AND METHODS: Individual patient data were pooled from 8 phase II and phase III trials evaluating first-line cisplatin-based combination chemotherapy in patients with metastatic urothelial carcinoma. Adverse events, treatment delivery, response proportions, and survival outcomes were compared between male and female patients. RESULTS: Of the 543 patients included in the analysis, 100 patients (18%) were women. There was no significant difference in the number of cycles of chemotherapy administered or in the proportions of patients experiencing severe toxicities when comparing male and female patients. There was no difference in the survival distributions between male and female patients (P = .08); the median survival of male patients was 11.7 months (95%
confidence interval [CI], 10.5-13.2) compared with 16.2 months for female patients (95% CI, 12.8-20.4). There was no significant difference in survival between men and women when controlling for baseline performance status and/or the presence of visceral metastases. CONCLUSION: Female patients with metastatic urothelial cancer tolerate cisplatin-based chemotherapy similarly to male patients and achieve comparable clinical outcomes. Although gender-associated survival disparities in patients with metastatic urothelial cancer cannot be completely ruled out, if such disparities exist, they are unlikely related to tolerability or efficacy of chemotherapy.

[1070]
TÍTULO / TITLE: - False Positive FDG PET/CT Resulting from Fibrous Dysplasia of the Bone in the Work-Up of a Patient with Bladder Cancer: Case Report and Review of the Literature.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Aras M; Ones T; Dane F; Nosheri O; Inanir S; Erdil TY; Turoglu HT
INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, Marmara University School of Medicine, Istanbul, Turkey.
RESUMEN / SUMMARY: - Fibrous dysplasia of the bone (FDB) is a common, genetic, developmental disorder with a benign course. FDB can be seen anywhere throughout the skeleton. It is usually asymptomatic and found incidentally on imaging studies that are performed for other purposes. Although whole body 18 F-flourodeoxyglucose PET/CT (FDG PET/CT) is widely used in tumor imaging, infections and benign pathologies like FDB may cause false positive results. Herein we report the case of a 48-year-old FDB patient with transitional cell carcinoma of the urinary bladder. Restaging FDG PET/CT showed multiple mild to moderate hypermetabolic bone lesions which were initially misinterpreted as bone metastases. In this case report, we aimed to guide physicians in evaluating bone lesions in cancer patients with FDB in the light of the literature.

[1071]
TÍTULO / TITLE: - Microvessel density and expression of vascular endothelial growth factor in clinically localized prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Luczynska E; Gasinska A; Wilk W
INSTITUCIÓN / INSTITUTION: - Anna Gasinska, Department of Applied Radiobiology, Centre of Oncology - Maria Sklodowska-Curie Memorial Institute,
RESUMEN / SUMMARY: Identifying biological differences between benign lesions and malignant prostatic cancer (PC) may facilitate precise indication for more aggressive post-operative treatment. Therefore, we examined immunohistochemically histological specimens from 140 PC patients treated with radical surgery. The mean age of the patients was 62.9 +/-6.2 (range 49.0-77.0) years. There were 13 (9.3%) at pTNM stage 1, 78 (55.7%) at stage 2, 40 (28.6%) at stage 3 and 9 (6.4%) at stage 4. In the analysed group there were 75 (53.6%) well differentiated, 53 (37.8 %) moderately differentiated and 12 (8.6%) poorly differentiated tumours. The mean pre-operative prostate-specific antigen (PSA) level was 9.9 +/-0.5 ng/ml. Concentration of serum PSA was significantly increased with pTNM stage (p = 0.011), Gleason score (p = 0.011) and tumour grade (p = 0.003). In 34 (24.3%) tumours vascular endothelial growth factor (VEGF) expression was not shown. In the analysed group of tumours the mean percentage of positive VEGF cells was 14.8 +/-1.4% and was not correlated with tumour grade (p = 0.648) or Gleason score (p = 0.697). However, significantly higher values for the protein were observed in pTNM 3 (p = 0.035) and pTNM 4 (P = 0.037) than in pTNM stage 1. In the whole series of tumours the mean microvessel density (MVD) was 97.5 +/-2.4 /mm². A non-significant decrease in the number of microvessels was observed in the highest pathological tumour volume (P = 0.631), Gleason score (p = 0.368) and tumour grade (p = 0.233). Prostate-specific antigen level was not associated statistically with either MVD (p = 0.466) or VEGF expression (p = 0.188). There was also no correlation between the immunohistochemical expression of VEGF and MVD (p = 0.925).

[1072]
TÍTULO / TITLE: Do patients with metastatic urothelial carcinoma benefit from docetaxel as second-line chemotherapy?
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: Clin Transl Oncol. 2013 Apr 20.
AUTORES / AUTHORS: Morales-Barrera R; Suarez C; Valverde C; Nunez I; Maldonado X; Morote J; Carles J
INSTITUCION / INSTITUTION: GU, CNS and Sarcoma Program, Department of Medical Oncology, Vall d’Hebron University Hospital, Universitat Autonoma Barcelona, Passeig Vall d’Hebron 119-129, 08035, Barcelona, Catalonia, España.
RESUMEN / SUMMARY: PURPOSE: To evaluate the efficacy and toxicity of docetaxel regimen as second-line after failure of a platinum-based
chemotherapy. METHODS: Between May 2005 and June 2008, we retrospectively analyzed the data of 22 patients who had evidence of disease progression after one prior platinum-based regimen for metastatic urothelial carcinoma. Patients were treated with two different docetaxel dose schedules: (1) docetaxel 60 mg/m² every 21 days for unfit patients or (2) docetaxel 75 mg/m² every 21 days for fit patients. RESULTS: Median number of docetaxel cycles was three. Overall disease control rate was 18%. Of the 22 patients, no patient achieved complete or partial response and four patients had stable disease. Median progression-free survival was 1.67 months and median overall survival was 3.12 months. Neutropenia was the most common adverse event. CONCLUSIONS: This study identifies that docetaxel as second-line chemotherapy has low activity and was associated with significant toxicity.

[1073]
TÍTULO / TITLE: Racial differences in social support and coping among family caregivers of patients with prostate cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1080/07347332.2013.778931

AUTORES / AUTHORS: Vines AI; Demissie Z

INSTITUCIÓN / INSTITUTION: a Department of Epidemiology, UNC Gillings School of Public Health, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.

RESUMEN / SUMMARY: More than 60 million Americans are informal caregivers to adults, which can negatively affect their health. Data from 126 White and 62 African American female caregivers in North Carolina were analyzed to describe social support and coping among family caregivers of patients with prostate cancer and to assess for racial differences. Social support amount and some coping methods differed by race. There was no racial difference in social support satisfaction. Borderline significant difference in social support by health status was found and this differed by race. These racial differences should be explored further to better understand the availability of caregiving resources and their health effects.

[1074]
TÍTULO / TITLE: Pyuria Predicts Poor Prognosis in Patients With Non-Muscle-Invasive Bladder Cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1016/j.clgc.2013.04.002
AUTORES / AUTHORS: - Azuma T; Nagase Y; Oshi M
INSTITUCIÓN / INSTITUTION: - Department of Urology, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan. Electronic address: azumamifune@yahoo.co.jp
RESUMEN / SUMMARY: - BACKGROUND: To evaluate the significance of inflammation in non-muscle-invasive bladder cancer (NMIBC), we assessed the presence of pyuria at time of diagnosis. PATIENTS AND METHODS: A cohort of 805 patients with newly diagnosed NMIBC between 1994 and 2007 at the Tokyo Metropolitan Tama Medical Center were enrolled in this retrospective study. Pyuria was defined as urine containing >/= 10 white blood cells (WBCs) per high power field (HPF). RESULTS: One hundred ninety-nine (24%) of the patients with NMIBC had pyuria. The 3-year recurrence-free survival rates of patients with and without pyuria were 10.9 vs. 45.0%, respectively. The 5-year progression-free survival rates of patients with and without pyuria were 72.3% and 95.7%, respectively. Multivariate Cox proportional hazards regression models indicated that pyuria was an independent predictor of disease recurrence and progression. After dividing the sample according to the European Organization for Research and Treatment of Cancer (EORTC) risk tables, we further classified patients into subgroups according to the presence of pyuria. The recurrence-free survival rates were higher in the pyuria-negative subgroups of the low, intermediate-low, intermediate-high, and high risk for recurrence groups. Similarly, the progression-free survival rates at 5 years were higher in the pyuria-negative subgroups of the low, intermediate-low, and intermediate-high risk for progression groups. CONCLUSION: Patients with inflammatory NMIBC exhibited poor clinical outcomes.

[1075]
TÍTULO / TITLE: - Older renal cell cancer patients experience increased rates of venous thromboembolic events: a retrospective cohort study of SEER-Medicare data.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
    ● Enlace al texto completo (gratuito o de pago) 1186/1471-2407-13-209
AUTORES / AUTHORS: - Connelly-Frost A; Shantakumar S; Kobayashi MG; Li H; Li L
RESUMEN / SUMMARY: - BACKGROUND: Venous thromboembolic co-morbidities can have a significant impact on treatment response, treatment options, quality of life, and ultimately, survival from cancer. The extent of venous thromboembolic co-morbidity among older renal cell cancer patients is poorly described in the literature. It is important to understand the scope of venous thromboembolic events, before and after diagnosis, in order to offer renal cell cancer patients optimal care and improved quality of life. METHODS: The main goal of this study was to estimate and describe the incidence of venous thromboembolic events before and after renal cell cancer diagnosis.
SEER-Medicare linked data (1991--2003) was utilized for this retrospective cohort analysis (n = 11,950) of older renal cell cancer patients (≥ 65 years). Incidence rates and proportions in addition to multivariable Cox proportional hazard and logistic regression models were utilized to describe the incidence and relative risk of venous thromboembolic events. RESULTS: We observed that in the 12 months after diagnosis, 8.3% of renal cell cancer patients experienced a deep venous thrombosis, 2.4% experienced a pulmonary embolism, and 3.9% experienced other thromboembolic events. Nearly 70% of venous thromboembolic events occurred in the first 90 days after renal cell cancer diagnosis. Renal cell cancer patients were 2.4 times more likely to have a venous thromboembolic event in the 12 months after cancer diagnosis than non-cancer patients followed during the same time frame. Recent history of a venous event substantially increased the risk of that same event in the 12 months after diagnosis (HR = 5.2-18.8). CONCLUSION: Venous thromboembolic events are common and serious co-morbidities that should be closely monitored in older renal cell cancer patients, particularly during the first 3 months following diagnosis and among those with a recent history of a venous thromboembolic event.
myoid cells in the tunica propria. Recent studies have shown that Bcrp is also expressed stage specifically and spatiotemporally by Sertoli and germ cells in the seminiferous epithelium of rat testes, limited only to a testis-specific cell adhesion ultrastructure known as the apical ectoplasmic specialisation (ES) in stage VI-early VIII tubules. These findings suggest that Bcrp is equipped by late spermatids and Sertoli cells to protect late-stage spermatids completing spermiogenesis. Furthermore, Bcrp was found to be associated with F (filamentous)-actin and several actin regulatory proteins at the apical ES and might be involved in the organisation of actin filaments at the apical ES in stage VII-VIII tubules. These findings will be carefully evaluated in this brief review.


[1077]
TÍTULO / TITLE: - Ultrasound detection of a renal mass in a patient with flank pain and hematuria.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
- Enlace al texto completo (gratuito o de pago) 5811/westjem.2012.8.12595
AUTORES / AUTHORS: - Marzec K; Mailhot T; Perera P
INSTITUCIÓN / INSTITUTION: - Los Angeles County + University of Southern California Medical Center, Department of Emergency Medicine, Los Angeles, California.
RESUMEN / SUMMARY: - Flank pain with hematuria is a common chief complaint in the emergency department (ED). Patients are often diagnosed with renal calculi or pyelonephritis and discharged with analgesics or antibiotics and follow-up. This case study describes a patient who presented to the ED with a 1 week history of flank pain and hematuria and was subsequently found to have a large renal mass on bedside ultrasound.

[1078]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Erdem H; Oktay M; Yildirim U; Uzunlar AK; Kayikci MA
INSTITUCIÓN / INSTITUTION: - Havva Erdem, Department of Pathology, Duzce University of Medical Faculty, Duzce, Turkey, e-mail: drhavvaerdem@hotmail.com.
The aim of this study was to investigate the relationship of AEG-1 and p53 with the prognostic parameters of renal cell carcinoma (RCC). In this study, 50 paraffin blocks were histopathologically diagnosed at the Department of Pathology of the Medical Hospital of Duzce University, between 2005 and 2011. The cases consisted of 24 clear cell (CC) and 26 non-clear cell (NCC) RCC subtypes as follows: 24 (48%) clear cell RCC, 12 (24%) papillary RCC, 4 (8%) multilocular cystic RCC and 10 (20%) chromophobe RCC; none had sarcomatoid changes. By immunohistochemical analysis we investigated AEG-1 and p53 expression in carcinomas of the kidney, and by statistical analysis determined their relationship with clinicopathological parameters. Significant relationships were found between increasing tumor diameter and the increase of p53 (p = 0.028). In addition, p53 was significantly related to renal sinus invasion (p = 0.05) and Fuhrman grade (p = 0.026). There was a significant relationship between increased AEG-1 staining scores and CC and NCC carcinoma subtypes (p = 0.032), tumor capsule invasion (p = 0.01) and lymphovascular invasion (p = 0.015). There was also a significant correlation between tumor size and capsule and lymphovascular invasion (p = 0.02). We concluded that high AEG-1 and p53 expression correlates with the prognostic parameters in RCC patients, and in addition may be associated with tumor progression.
The most severe complication of yttrium-90 therapy is gastrointestinal ulceration caused by extrahepatic dispersion of microspheres. Standard pretreatment planning requires extensive angiographic evaluation of the hepatic circulation and embolization of hepatoenteric collaterals; however, in patients with severe renal insufficiency, this evaluation may lead to acute renal failure. In order to minimize iodinated contrast utilization in a patient with preexisting severe renal insufficiency, the authors describe the use of a balloon catheter for temporary occlusion of the common hepatic artery to induce transient redirection of flow of the hepatoenteric arteries towards the liver, in lieu of conventional coil embolization.

[1081]
TÍTULO / TITLE: - Clinical uncertainty of prostate cancer genetic risk panels.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
    ●●Enlace al texto completo (gratuito o de pago) 1126/scitranslmed.3004696
AUTORES / AUTHORS: - Pomerantz M; Freedman ML
INSTITUCIÓN / INSTITUTION: - Mark Pomerantz, M.D. is a Medical Oncologist at the Dana-Farber Cancer Institute, Boston, MA 02115, USA.

[1082]
TÍTULO / TITLE: - Can Western based online prostate cancer risk calculators be used to predict prostate cancer after prostate biopsy for the Korean population?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
    ●●Enlace al texto completo (gratuito o de pago) 3349/ymj.2013.54.3.665
AUTORES / AUTHORS: - Lee DH; Jung HB; Park JW; Kim KH; Kim J; Lee SH; Chung BH
INSTITUCIÓN / INSTITUTION: - Department of Urology, Urological Science Institute, Gangnam Severance Hospital, Yonsei University College of Medicine, 211 Eonju-ро, Gangnam-gu, Seoul 135-720, Korea.
RESUMEN / SUMMARY: - PURPOSE: To access the predictive value of the European Randomized Screening of Prostate Cancer Risk Calculator (ERSPC-RC) and the Prostate Cancer Prevention Trial Risk Calculator (PCPT-RC) in the Korean population. MATERIALS AND METHODS: We retrospectively analyzed
the data of 517 men who underwent transrectal ultrasound guided prostate biopsy between January 2008 and November 2010. Simple and multiple logistic regression analysis were performed to compare the result of prostate biopsy. Area under the receiver operating characteristics curves (AUC-ROC) and calibration plots were prepared for further analysis to compare the risk calculators and other clinical variables. RESULTS: Prostate cancer was diagnosed in 125 (24.1%) men. For prostate cancer prediction, the area under curve (AUC) of the ERSPC-RC was 77.4%. This result was significantly greater than the AUCs of the PCPT-RC and the prostate-specific antigen (PSA) (64.5% and 64.1%, respectively, p<0.01), but not significantly different from the AUC of the PSA density (PSAD) (76.1%, p=0.540). When the results of the calibration plots were compared, the ERSPC-RC plot was more constant than that of PSAD. CONCLUSION: The ERSPC-RC was better than PCPT-RC and PSA in predicting prostate cancer risk in the present study. However, the difference in performance between the ERSPC-RC and PSAD was not significant. Therefore, the Western based prostate cancer risk calculators are not useful for urologists in predicting prostate cancer in the Korean population.

[1083]

TITULO / TITLE: - Effect of Transurethral Resection of the Prostate on Storage Symptoms in Patients with Benign Prostatic Hyperplasia of Less than 30 ml.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Kang YJ; Kim KH; Seo Y; Lee KS

INSTITUCIÓN / INSTITUTION: - Department of Urology, College of Medicine, Dongguk University, Gyeongju, Korea.

RESUMEN / SUMMARY: - PURPOSE: Many patients with benign prostatic hyperplasia (BPH) have not only voiding symptoms but also storage symptoms. Despite the many types of treatment that have been developed for BPH, storage symptoms persist. We conducted an assessment of the efficacy of transurethral resection of the prostate (TURP) and the change in the International Prostate Symptoms Score (IPSS) storage sub-score after the procedure according to prostate size in patients with BPH. MATERIALS AND METHODS: Men aged 50 years or older who had BPH were enrolled in this study. 186 patients were divided into two groups according to prostate size measuring using transrectal ultrasonography: In group 1, prostate size was less than 30 ml (51 patients), and in group 2, prostate size was greater than 30 ml (135 patients). All of the patients underwent TURP. We examined whether the degree of change in the IPSS, voiding symptoms, storage symptoms, and quality of life (QoL) differed before and after TURP and according to prostate size.
size. RESULTS: After three months of TURP, the subjects in both groups showed significant improvement in the IPSS, voiding symptoms, storage symptoms, QoL, and maximum flow rate (p<0.05). The scores for the IPSS, voiding symptoms, storage symptoms, and QoL of group 1 and 2 after three months of TURP were 16.36, 14.25 (p=0.233), 8.21, 8.24 (p=0.980), 8.11, 5.16 (p=0.014), 2.89, and 2.10 (p=0.030), respectively. CONCLUSIONS: TURP is an effective treatment for patients with BPH, regardless of prostate size. However, while the improvement in the storage symptoms of patients with a prostate size of less than 30 ml was not significant, it was in patients with a prostate size greater than 30 ml.

[1084]

TÍTULO / TITLE: - PARP inhibition sensitizes to low dose-rate radiation
TMPRSS2-ERG fusion gene-expressing and PTEN-deficient prostate cancer cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Chatterjee P; Choudhary GS; Sharma A; Singh K; Heston WD; Ciezki J; Klein EA; Almasan A

INSTITUCIÓN / INSTITUTION: - Department of Cancer Biology, Lerner Research Institute, Cleveland Clinic, Cleveland, OH, USA.

RESUMEN / SUMMARY: - Exposure to genotoxic agents, such as irradiation produces DNA damage, the toxicity of which is augmented when the DNA repair is impaired. Poly (ADP-ribose) polymerase (PARP) inhibitors were found to be “synthetic lethal” in cells deficient in BRCA1 and BRCA2 that impair homologous recombination. However, since many tumors, including prostate cancer (PCa) rarely have on such mutations, there is considerable interest in finding alternative determinants of PARP inhibitor sensitivity. We evaluated the effectiveness of radiation in combination with the PARP inhibitor, rucaparib in PCa cells. The combination index for clonogenic survival following radiation and rucaparib treatments revealed synergistic interactions in a panel of PCa cell lines, being strongest for LNCaP and VCaP cells that express ETS gene fusion proteins. These findings correlated with synergistic interactions for senescence activation, as indicated by beta—galactosidase staining. Absence of PTEN and presence of ETS gene fusion thus facilitated activation of senescence, which contributed to decreased clonogenic survival. Increased radiosensitivity in the presence of rucaparib was associated with persistent DNA breaks, as determined by chi-H2AX, p53BP1, and Rad51 foci. VCaP cells, which harbor the TMPRSS2-ERG gene fusion and PC3 cells that stably express a similar construct (fusion III) showed enhanced sensitivity towards rucaparib, which, in
turn, increased the radiation response to a similar extent as the DNA-PKcs inhibitor NU7441. Rucaparib radiosensitized PCa cells, with a clear benefit of low dose-rate radiation (LDR) administered over a longer period of time that caused enhanced DNA damage. LDR mimicking brachytherapy, which is used successfully in the clinic, was most effective when combined with rucaparib by inducing persistent DNA damage and senescence, leading to decreased clonogenic survival. This combination was most effective in the presence of the TMPRSS2-ERG and in the absence of PTEN, indicating clinical potential for brachytherapy in patients with intermediate and high risk PCa.

[1085]

TÍTULO / TITLE: - Pre-radiotherapy PSA Level as a Predictor for Biochemical Control in Prostate Cancer Patients Receiving Radiotherapy after Radical Prostatectomy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Tsan DL; Fan KH; Chen YC; Chuang CK; Lee CC; Hong JH
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Taoyuan, Taiwan.
RESUMEN / SUMMARY: - Background: To report the outcome of patients receiving radiotherapy (RT) after radical prostatectomy (RP). Methods: Between May 2001 and December 2008, 53 consecutive cases of prostate adenocarcinoma treated with RP and RT were reviewed. Results: A total of 49 patients were eligible for this study. After a median follow-up of 53 months, the 4-year overall survival (OS) and biochemical progression-free survival (bPFS) for all patients were 91.0% and 68.9%, respectively. According to univariate and multivariate analysis, pre-RT prostate-specific antigen (PSA) was the most significant factor for bPFS. Patients with pre-RT PSA levels of < 0.2 ng/ml and >= 0.2 ng/ml had a 4-year bPFS of 83.1% and 52.6%, respectively (p = 0.013). The incidence of chronic rectal toxicity was low, with no grade 3 toxicity reported and grade 2 toxicity found in only 6 patients (12.2%). However, long-term urinary toxicity of grade 2 or higher was found in 24 patients (49.0%). Conclusion: For patients with increasing PSA levels following RP, local RT should be administered prior to biochemical failure (PSA >= 0.2), to ensure good bPFS.

[1086]

TÍTULO / TITLE: - Global advances in prostate cancer diagnosis and therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Dosimetric effects of weight loss or gain during volumetric modulated arc therapy and intensity-modulated radiation therapy for prostate cancer.

Weight loss or gain during the course of radiation therapy for prostate cancer can alter the planned dose to the target volumes and critical organs. Typically, source-to-surface distance (SSD) measurements are documented by therapists on a weekly basis to ensure that patients’ exterior surface and isocenter-to-skin surface distances remain stable. The radiation oncology team then determines whether the patient has undergone a physical change sufficient to require a new treatment plan. The effect of weight change (SSD increase or decrease) on intensity-modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT) dosimetry is not well known, and it is unclear when rescanning or replanning is needed. The purpose of this study was to determine the effects of weight change (SSD increase or decrease) on IMRT or VMAT dose delivery in patients with prostate cancer and to determine the SSD change threshold for replanning. Whether IMRT or VMAT provides better dose stability under weight change conditions was also determined. We generated clinical IMRT and VMAT prostate and seminal vesicle treatment plans for varying SSDs for 10 randomly selected patients with prostate cancer. The differences due to SSD change were quantified by a specific dose change for a specified volume of interest. The target mean dose, decreased or increased by 2.9% per 1-cm SSD decrease or increase in IMRT and by 3.6% in VMAT. If the SSD deviation is more than 1cm, the radiation oncology team should determine whether to continue treatment without modifications, to adjust monitor units, or to resimulate and replan.
TITULO / TITLE: - Urine screening by Seldi-Tof, followed by biomarker identification, in a Brazilian cohort of patients with Renal Cell Carcinoma (RCC).

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Alves G; Pereira DA; Sandim V; Ornellas AA; Escher N; Melle C; von Eggeling F

INSTITUCIÓN / INSTITUTION: - Applied Genetic Laboratory, Hematology Division, National Institute of Cancer; Division of Urology, National Institute of Cancer; Division of Urology, Hospital Mario Kroeff, Rio de Janeiro, RJ, Brazil; Core Unit Chip Application, Institute of Human Genetics, Jena University Hospital, Jena; Alere Technologies GmbH, Jena and Biomolecular Photonics Group, Jena University Hospital, Germany.

RESUMEN / SUMMARY: - Purpose: To screen proteins/peptides in urine of Renal Cell Carcinoma (RCC) patients by SELDI-TOF (Surface Enhanced Laser Desorption Ionization - Time of Flight) in search of possible biomarkers. Material and Methods: Sixty-one urines samples from Clear Cell RCC and Papillary RCC were compared to 29 samples of control urine on CM10 chip. Mass analysis was performed in a ProteinChip Reader PCS 4,000 (Ciphergen Biosystems, Fremont, CA) with the software Ciphergen Express 3.0. All chips were read at low and at high laser energy. For statistical analysis the urine samples were clustered according to the histological classification (Clear Cell and Papillary Carcinoma). For identification urine was loaded on a SDS PAGE gel and bands of most interest were excised, trypsinized and identified by MS/MS. Databank searches were performed in Swiss-Prot database using the MASCOT search algorithm and in Profound. Results: Proteins that were identified from urine of controls included immunoglobulin light chains, albumin, secreted and transmembrane 1 precursor (protein K12), mannan-binding lectin-associated serine protease-2 (MASP-2) and vitelline membrane outer layer 1 isoform 1. Identification of immunoglobulins and isoforms of albumin are quite common by proteomics and therefore cannot be considered as possible molecular markers. K12 and MASP-2 play important physiological roles, while vitellite membrane outer layer 1 role is unknown since it was never purified in humans. Conclusions: The down expression of Protein K-12 and MASP-2 make them good candidates for RCC urine marker and should be validated in a bigger cohort including the other less common histological RCC subtypes.

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TITULO / TITLE: - Ureteroiliac fistula secondary to radiotherapy in a patient with single renal metastasis of colon adenocarcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 5489/cuaj.259
AUTORES / AUTHORS: - Dormeus S; Hernandez EA; Nicolazzi M; Barba JF; Algarra R; Tienza A; Pascual JI; Berian JM; Zudaire JJ
INSTITUCIÓN / INSTITUTION: - Universite Catholique de Louvain, Belgium;
RESUMEN / SUMMARY: - We report the case of a 61-year-old man diagnosed in 2001 with rectal cancer (stage T3N1M0). The patient was treated with surgery, adjuvant chemotherapy and radiotherapy. In 2009, he was admitted to the urology department with a complaint of right hemiabdominal pain. The anatomopathological investigation reported renal metastasis of colon adenocarcinoma. After surgery, he received adjuvant chemotherapy. No tumour recurrence or metastasis was reported at the 22-month follow-up.
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[1090]
TÍTULO / TITLE: - Metabolic Syndrome as a Peculiar Target for Management of Prostate Cancer Patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1016/j.clgc.2013.04.009
AUTORES / AUTHORS: - Conteduca V; Di Lorenzo G; Bozza G; Ardito R; Aieta M
INSTITUCIÓN / INSTITUTION: - Centro di Riferimento Oncologico della Basilicata IRCCS, Rionero in Vulture, Italy. Electronic address: cinzia.conteduca@libero.it.
RESUMEN / SUMMARY: - An interesting and reciprocal association between the metabolic syndrome and prostate cancer has been identified. Metabolic alterations, such as hyperinsulinemia, increased levels of insulin growth factor-1, and insulin resistance could be on the basis of development and progression of many tumors, including prostate cancer, and changes in body composition, in turn, can represent some side effects of androgen deprivation therapy and novel drugs, such as mammalian target of rapamycin inhibitors. This review evaluates this interrelation between metabolic syndrome and prostate tumor scanning in many clinical and preclinical epidemiological studies and describes possible pathogenetic biological mechanisms. Finally, this article discusses feasible clinical implications for the management, prevention, diagnosis, prognosis, and treatment of patients affected by metabolic syndrome and prostate cancer, with particular attention to the metformin action.
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[1091]
TÍTULO / TITLE: - Clinico-Pathologic Characterisation of metastatic prostate cancer in the Radiotherapy and Oncology Department, Ahmadu Bello University Teaching Hospital, Zaria - Nigeria: 2006 - 2009.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AIMS AND OBJECTIVES: To evaluate the Clinico-pathologic Characteristics of Metastatic prostate cancer patients seen in the Radiotherapy and Oncology Department, Ahmadu Bello University Teaching Hospital Zaria, Nigeria. MATERIALS AND METHODS: Between January 2006 and December 2009, a period of 4 years, 72 new patients with prostate cancers were seen of which 43 patients had distant metastases. Only patients with histologic confirmation of prostate cancer and having metastases were included in the study irrespective of age, co-morbidity and performance status. Patients’ folders were reviewed retrospectively with a structured pro forma. Information retrieved from patient’s folder included age, histology, Gleason score, co-morbidities, interval between diagnosis and referral to oncology unit, interval between referral and presentation at oncology unit, PSA at diagnosis and presentation at oncology unit, sites of metastases, bones sites involved in bone metastases, types of treatment received and follow up status. Results were analysed using Epi Info software Version 3.4.1; 2007 Edition. RESULTS: 43 patients had distant metastases from prostate cancer during initial evaluation at presentation in the radiotherapy and oncology centre. The mean age was 66.2 years (range, 47 – 82 years, median age 66 years and modal age group was 65 - 69 years). Co-morbidity was seen in 18 patients, with hypertension being the commonest (HT = 14, DM = 2 and HIV 2 patients). No morbidity seen in 25 patients. The range of duration from diagnosis to referral was 1 - 84 months. Only 20 patients presented at radiotherapy and oncology centre within 6 months of diagnosis and 18 patients presented after 12 months of diagnosis. 33 patients presented within 1 month of being referred for further management. 6 patients reported within 2 months and 2 patients within 3 months and another 2 patients within 4 months. Only 27 patients had PSA done at diagnosis. No PSA was done in 16 patients. The PSA range at diagnosis was 10.0 - 232 ng/ml, mean PSA was 67.46 ng/ml while only 40 patients did PSA on presentation for further management with a range of 1 - 245 ng/ml and a mean of 57.95 ng/ml. The histology report revealed adenocarcinoma and transitional carcinoma in 42 and 1 patients respectively. The Gleason score range was 6 - 10, with a mean score of 7.8. The Gleason score was not reported in 3 patients. Multiple organs involvement by metastases was seen in 16 patients. Bone metastases was the commonest (35), followed by lungs (8), liver (7), Virchow’s lymph nodes (6), brain (5), and soft tissue (5). The lumbar vertebrae was the commonest site of bone metastases (32) followed by the sacrum (17), pelvis (11), and long bones (7). 3 patients had metastases to the ribs and 2 patients each to the skull, sternum and cervical.
PURPOSE: We examined the serum levels of testosterone (T) (total and bioavailable) dehydroepiandrosterone (DHEA), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prostate-specific antigen (PSA) in men receiving treatment with luteinizing hormone releasing-hormone (LHRH) agonists for metastatic prostate cancer. In doing this, we want to determine the efficacy of these agents in lowering T levels and whether a possible relationship exists between PSA values, as a surrogate measure of tumour activity, and hormone levels.

METHODS: This was a single centre prospective study of patients on LHRH agonists. Of all the 100 eligible patients, 31 did not qualify (10 were receiving their first injection, 13 were on intermittent hormonal therapy, 7 refused to enter the trial and 1 patient’s blood sample was lost). Therefore in total, 69 patients were included in the final analysis. Each patient had their blood sample drawn immediately before the administration of a LHRH agonist. The new proposed criteria of <20 ng/dL (0.69 nmol/L) of total testosterone was used to define optimal levels of the hormone in this population.

RESULTS: Of the 69 patients, 41 were on goserelin injections, 21 on leuprolide, and 7 on buserelin. There was no statistical difference in hormone levels between any of the medications. Overall, 21% of patients failed to reach optimal levels of total testosterone. PSA levels were higher in this group. There was a statistically significant correlation between PSA and testosterone levels, as well as between PSA and FSH. Serum levels of PSA, however, did not correlate with those of bioavailable testosterone.

CONCLUSIONS: Failure to reach optimal levels of testosterone occurs in patients on LHRH agonist therapy. Higher PSA values are more commonly found in patients with suboptimal levels of testosterone receiving LHRH analogs, but the clinical importance of this finding has not been established. There is no significant difference with respect to hormonal levels reached among patients on a variety of LHRH agonists. Total testosterone determinations should be considered in patients on LHRH agonist therapy, particularly when the PSA values begin to rise since it may lead to further beneficial hormonal manipulation.
TÍTULO / TITLE: - Neoadjuvant chemotherapy improves survival rate in advanced urothelial carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Tsai CC; Huang CH; Huang CN; Wu WJ; Yeh HC; Li WM; Li CC; Lee MH
INSTITUCIÓN / INSTITUTION: - Department of Urology, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan.
RESUMEN / SUMMARY: - Radical surgery (RS) with adjuvant chemotherapy (AC) or radiotherapy has been conventionally used for patients with advanced urothelial carcinoma (AUC). Recent research has indicated that systemic neoadjuvant chemotherapy (NC) with RS yields better outcomes than RS alone for patients with locally advanced bladder cancer. However, there are no reports indicating whether NC or AC would be beneficial for patients with AUC. The present study compared the survival rate for AUC patients receiving NC or AC. A retrospective analysis was conducted using data for 64 patients with AUC who underwent RS and systemic chemotherapy at our institution between March 2002 and March 2011. Of the 64 patients, 30 received NC before RS and 34 received RS followed by systemic AC. Pathologic stages (p=0.002), grades (p=0.018) and lymphovascular invasion (p=0.047) were significantly lower in the patients who received NC first than in those who received RC first. Furthermore, analysis of the surgical specimens revealed that 26.7% of patients who received NC before RS had complete remission. There were no significant differences in demographic data, surgical complications, and chemotoxicity between the two patient groups. The progression-free survival (PFS) and overall survival (OS) of patients who received initial NC were significantly better than those of patients who received initial RC (p=0.002 and 0.018, respectively). Our results indicate that NC administration before RS significantly improved the PFS and OS of AUC patients, without increasing surgical complications and chemotoxicity. Further prospectively controlled trials need to be conducted to confirm the effectiveness of NC for AUC patients.

Gross hematuria in patients with prostate cancer: etiology and management.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
The objective of the study is to assess the etiology and prognosis of gross hematuria (GH) in patients with carcinoma of the prostate (CAP). From 1991 to 2011, 81 men (mean age 74.3 years, SD 6.5) with CAP were hospitalized with GH. Primary treatment of CAP was radical surgery in 13 patients (group 1) and nonsurgical therapy in 68 (group 2), mostly radiotherapy (35 cases) and hormonal treatment (25 cases). The common etiologies of GH in group 1 were bladder cancer (38.5%) and urinary infection (23%). In contrast, CAP itself caused GH in 60% of the patients in group 2. Thirty-nine patients (48%) required transurethral surgery to manage GH which was effective in all cases; nevertheless, the prognosis of group 2 patients was dismal with median overall survival of 13 months after sustaining hematuria, compared to 50 months in group 1 (P = 0.0015). We conclude that the etiology of GH in patients with CAP varies according to primary treatment. After radical prostatectomy, it is habitually caused by bladder cancer or infection. When the primary treatment is not surgical, GH is most commonly due to CAP itself. Although surgical intervention is effective in alleviating hematuria of these patients, their prognosis is dismal.

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[1095]
TÍTULO / TITLE: - Prostate cancer: Does a negative second biopsy give patients false hope?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Clyne M

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[1096]
TÍTULO / TITLE: - Biopsy-proven drug-induced tubulointerstitial nephritis in a patient with acute kidney injury and alcoholic severe acute pancreatitis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Yoshioka W; Mori T; Nagahama K; Tamura T
INSTITUCIÓN / INSTITUTION: - Department of Nephrology, Yokosuka Kyosai Hospital, Yokosuka, Japan.

RESUMEN / SUMMARY: - We report a 49-year-old man with alcoholic severe acute pancreatitis (SAP) complicated by drug-induced acute tubulointerstitial nephritis (DI-AIN). Oliguria persisted and became anuric again on day 17 despite improvement of pancreatitis. He presented rash, fever and eosinophilia from day 20. Renal biopsy was performed for dialysis-dependent acute kidney injury (AKI), DI-AIN was revealed, and prompt use of corticosteroids fully restored his renal function. This diagnosis might be missed because it is difficult to perform renal biopsy in such a clinical situation. If the patient’s general condition allows, renal biopsy should be performed and reversible AKI must be distinguished from many cases of irreversible AKI complicated by SAP. This is the first report of biopsy-proven DI-AIN associated with SAP, suggesting the importance of biopsy for distinguishing DI-AIN in persisting AKI of SAP.

[1097]

TÍTULO / TITLE: - Cabazitaxel in Patients With Metastatic Castration-Resistant Prostate Cancer: Results of a Compassionate Use Program in The Netherlands.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Wissing MD; van Oort IM; Gerritsen WR; van den Eertwegh AJ; Coenen JL; Bergman AM; Gelderblom H

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Leiden University Medical Center, Leiden, the Netherlands.

RESUMEN / SUMMARY: - BACKGROUND: Cabazitaxel has been reimbursed as a second-line therapy for patients with metastatic castrate-resistant prostate cancer (mCRPC) in the Netherlands since 2011. Before reimbursement was available, cabazitaxel was provided through a Compassionate Use Program (CUP). We report the results of the Dutch CUP, detailing the safety and efficacy of cabazitaxel in a routine clinical practice setting. PATIENTS AND METHODS: Safety and efficacy data of all 5 Dutch centers participating in the cabazitaxel CUP were collected. Safety data were collected prospectively using the National Cancer Institute Common Toxicity Criteria for Adverse Events, version 3.0. Overall survival (OS) and progression-free survival (PFS), time to PSA progression (TTPP), and best clinical response were evaluated retrospectively. RESULTS: Fifty-one patients were registered in the CUP; 49 received cabazitaxel. Forty-two of 49 patients [85.7%], 42 patients had >/= 2 metastatic sites. Patients received on average 6 cabazitaxel cycles (range, 1-21). A dose reduction or dose delay occurred in 13 and 20 patients [26.5% and 40.9%] respectively. Prophylactic granulocyte colony-stimulating factor (G-CSF) was...
used in 8 patients [16.3%]. Grade >/= 3 adverse events were observed in 25 patients [51.0%]; 16 patients [32.7%] discontinued treatment because of treatment-emergent adverse events (TEAEs). Serious adverse events (SAEs) occurred in 16 (32.7%) patients; the most frequent SAEs were hematuria (4 patients [8.3%]) and urosepsis (3 patients [6.3%]). Febrile neutropenia occurred twice; no patient had grade >/= 3 neuropathy. No toxicity-related mortality occurred. Median follow-up was 24.1 months. Median OS was 8.7 months (interquartile range [IQR], 6.0-15.9 months); median TTP was 2.8 months (IQR, 1.7-5.9 months). CONCLUSION: In the Dutch CUP, patients with advanced mCRPC had delayed tumor progression with acceptable toxicities using cabazitaxel treatment.

[1098]
TITLE: Plasma miRNAs as Biomarkers to Identify Patients with Castration-Resistant Metastatic Prostate Cancer.
SUMMARY: MicroRNAs (miRNAs) have emerged as key regulators of numerous biological processes, and increasing evidence suggests that circulating miRNAs may be useful biomarkers of clinical disease. In this study, we sought to identify plasma miRNAs that differentiate patients with metastatic castration resistant prostate cancer (mCRPC) from those with localized prostate cancer (PCa). Pooled plasma samples from patients with localized PCa or mCRPC (25 per group) were assayed using the Exiqon miRNA qPCR panel, and the differential expression of selected candidates was validated using qRT-PCR. We identified 63 miRNAs upregulated in mCRPC versus localized PCa, while only four were downregulated. Pearson’s correlation analysis revealed two highly correlated groups: one consisting of miR-141, miR375 and miR-200c and the other including miR151-3p, miR423-3p, miR-126, miR152 and miR-21. A third group, containing miR-16 and miR-205, showed less correlation. One miRNA from each group (miR-141, miR151-3p and miR-16) was used for logistic regression analysis and proved to increase the sensitivity of the prostate-specific antigen (PSA) test alone. While no miRNA alone differentiated localized PCa and mCRPC, combinations had greater sensitivity and specificity. The expression of these 10 candidates was assayed for association with clinical parameters of disease progression through the cBio
portal. Our results demonstrate that plasma levels of selected miRNAs are potential biomarkers to differentiate localized PCa and mCRPC.

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[1099]

**TÍTULO / TITLE:** - Erratum to: Bortezomib represses HIF-1alpha protein expression and nuclear accumulation by inhibiting both PI3K/Akt/TOR and MAPK pathways in prostate cancer cells.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1007/s00109-013-1030-4

**AUTORES / AUTHORS:** - Befani CD; Vlachostergios PJ; Hatzidaki E; Patrikidou A; Bonanou S; Simos G; Papandreou CN; Liakos P

**INSTITUCIÓN / INSTITUTION:** - Laboratory of Biochemistry, Faculty of Medicine, University of Thessaly, Biopolis, 41110, Larissa, Greece.

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[1100]

**TÍTULO / TITLE:** - Differential cytotoxic activity of a novel palladium-based compound on prostate cell lines, primary prostate epithelial cells and prostate stem cells.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0064278

**AUTORES / AUTHORS:** - Ulukaya E; Frame FM; Cevatemre B; Pellacani D; Walker H; Mann VM; Simms MS; Stower MJ; Yilmaz VT; Maitland NJ

**INSTITUCIÓN / INSTITUTION:** - Department of Medical Biochemistry, Medical School, Uludag University, Bursa, Turkey.

**RESUMEN / SUMMARY:** - The outcome for patients with advanced metastatic and recurrent prostate cancer is still poor. Therefore, new chemotherapeutics are required, especially for killing cancer stem cells that are thought to be responsible for disease recurrence. In this study, we screened the effect of a novel palladium-based anticancer agent (Pd complex) against six different prostate cancer cell lines, and primary cultures from seven Gleason 6/7 prostate cancer, three Gleason 8/9 prostate cancer and four benign prostate hyperplasia patient samples, as well as cancer stem cells selected from primary cultures. MTT and ATP viability assays were used to assess cell growth and flow cytometry to assess cell cycle status. In addition, immunofluorescence was used to detect gammaH2AX nuclear foci, indicative of DNA damage, and Western blotting to assess the induction of apoptosis and autophagy. The Pd complex showed a powerful growth-inhibitory effect against both cell lines and
primary cultures. More importantly, it successfully reduced the viability of cancer stem cells as first reported in this study. The Pd complex induced DNA damage and differentially induced evidence of cell death, as well as autophagy. In conclusion, this novel agent may be promising for use against the bulk of the tumour cell population as well as the prostate cancer stem cells, which are thought to be responsible for the resistance of metastatic prostate cancer to chemotherapy. This study also indicates that the combined use of the Pd complex with an autophagy modulator may be a more promising approach to treat prostate cancer. In addition, the differential effects observed between cell lines and primary cells emphasise the importance of the model used to test novel drugs including its genetic background, and indeed the necessity of using cells cultured from patient samples.

[1101]

TÍTULO / TITLE: - Tumor associated copy number changes in the circulation of patients with prostate cancer identified through whole-genome sequencing.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Heitzer E; Ulz P; Belic J; Gutschi S; Quehenberger F; Fischereder K; Benezeder T; Auer M; Pischler C; Mannweiler S; Pichler M; Eisner F; Haeusler M; Riethdorf S; Pantel K; Samonigg H; Hoefler G; Augustin H; Geigl JB; Speicher MR

RESUMEN / SUMMARY: - BACKGROUND: Patients with prostate cancer may present with metastatic or recurrent disease despite initial curative treatment. The propensity of metastatic prostate cancer to spread to the bone has limited repeated sampling of tumor deposits. Hence, considerably less is understood about this lethal metastatic disease, as it is not commonly studied. Here we explored whole-genome sequencing of plasma DNA to scan the tumor genomes of these patients noninvasively. METHODS: We wanted to make whole-genome analysis from plasma DNA amenable to clinical routine applications and developed an approach based on a benchtop high-throughput platform, i.e. Illumina’s MiSeq instrument. We performed whole-genome sequencing from plasma at a shallow sequencing depth to establish a genome-wide copy number profile of the tumor at low costs within 2 days. In parallel, we sequenced a panel of 55 high-interest genes and 38 introns with frequent fusion breakpoints such as the TMPRSS2-ERG fusion with high coverage. After intensive testing of our approach with samples from 25 individuals without cancer we analyzed 13 plasma samples derived from 5 patients with castration resistant (CRPC) and 4 patients with castration sensitive prostate cancer (CSPC). RESULTS: The genome-wide profiling in the plasma of our patients revealed multiple copy number aberrations including those previously reported in prostate tumors, such as losses in 8p and gains in 8q. High-level copy
number gains in the AR locus were observed in patients with CRPC but not with CSPC disease. We identified the TMPRSS2-ERG rearrangement associated 3-Mbp deletion on chromosome 21 and found corresponding fusion plasma fragments in these cases. In an index case multiregional sequencing of the primary tumor identified different copy number changes in each sector, suggesting multifocal disease. Our plasma analyses of this index case, performed 13 years after resection of the primary tumor, revealed novel chromosomal rearrangements, which were stable in serial plasma analyses over a 9 months period, which is consistent with the presence of one metastatic clone. CONCLUSIONS: The genomic landscape of prostate cancer can be established by non-invasive means from plasma DNA. Our approach provides specific genomic signatures within 2 days which may therefore serve as “liquid biopsy”.

[1102]

TÍTULO / TITLE: - Predictive preoperative factors for renal insufficiency in patients followed for more than 5 years after radical nephrectomy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ahn JS; Kim HJ; Jeon HG; Jeong BC; Seo SI; Lee HM; Choi HY; Jeon SS

INSTITUCIÓN / INSTITUTION: - Department of Urology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - PURPOSE: We assessed the predictive factors for renal insufficiency in patients followed for more than 5 years after radical nephrectomy. MATERIALS AND METHODS: Age, gender, history of diabetes, history of hypertension, body mass index, preoperative estimated glomerular filtration rate (eGFR), serum uric acid, urine albumin, normal renal parenchymal volume, tumor size, and ratio of normal parenchymal volume of the removed kidney to that of the remaining kidney were evaluated retrospectively in 89 patients who underwent radical nephrectomy from January 2001 to December 2005. Patients were included whose renal parenchymal volume was measurable by use of perioperative imaging (computed tomography or magnetic resonance imaging), whose preoperative eGFR was greater than 60 mL/min/1.73 m(2), and who were followed for more than 5 years. To measure renal parenchymal volume from imaging, we integrated the extent of the normal renal parenchyma from axial slides of images. RESULTS: In univariate and multivariate binary regression analysis, the parenchymal volume of the remnant kidney (p=0.001), a history of diabetes (p=0.035), and preoperative eGFR (p=0.011) were independent factors for renal insufficiency. By use of a receiver operating characteristic curve, a volume of 170 mL was determined to be an
appropriate cutoff value, with sensitivity of 58.7% and specificity of 74.4% for the parenchymal volume of the remnant kidney for predicting eGFR less than 60 mL/min/1.73 m(2) (area under the curve, 0.678). The parenchymal volume of the remnant kidney was also an independent factor for the downgrading of the chronic kidney disease category in the multivariate linear regression analysis (p=0.021). CONCLUSIONS: Preoperative eGFR, a history of diabetes, and the radiologic volume of the remaining kidney parenchyma could be useful factors for predicting postoperative renal function. Patients with parenchymal volumes of less than 170 mL have a higher risk of postoperative renal insufficiency, which should be considered carefully when choosing a treatment modality.

[1103]

TITULO / TITLE: Study of testosterone as a predictor of tumor aggressiveness in patients with prostate cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Cabral PH; Iwamoto MW; Fanni VS; Barros Lda R; Cardoso SN; Mello LF; Glina S
INSTITUCIÓN / INSTITUTION: Ipiranga Hospital, Department of Urology and Brazilian Institute of Cancer Control - IBCC Sao Paulo, Brazil.
RESUMEN / SUMMARY: Purpose: A growing body of evidence suggests that low testosterone can be an independent predictor of adverse clinicopathological features and worse prognosis in prostate cancer (PCa) patients. However, this association is still incompletely understood and the results are divisive. The aim of this study was to analyze testosterone as a predictor of aggressive disease in subjects with clinically localized PCa. Materials and Methods: A cohort was conducted including the patients submitted to radical prostatectomy in our institution during a period of four years. The patients had clinically localized disease and their total testosterone (TT) was routinely measured preoperatively in the morning before surgery. They were stratified in groups with low (< 300 ng/dL) and normal TT (/>= 300 ng/dL). Tumor aggressiveness was inferred based on preoperative PSA levels, pathological Gleason score (lower, equal or greater than 7), TNM stage and surgical margins status. Results: After analyzing 164 patients we found a significant association between mean preoperative TT and extraprostatic disease (379 for pT3 vs. 421 ng/for pT2 - p < 0.001, AUC > 0.99). Conversely, men with high Gleason score had similar mean TT compared to those with lower scores. Preoperative low TT (defined as TT < 300 ng/dL) could not be statistically correlated with either preoperative PSA levels, pathological Gleason score, extraprostatic extension, positive surgical margins or seminal vesicles involvement. Conclusions: This study indicates that testosterone may be a useful predictive tool once pathological extraprostatic extension was somewhat signaled by lower TT levels.
preoperatively. However, it does not consolidate a clear association between aggressive tumor biology and hypogonadism.

[1104]
**TÍTULO / TITLE:** Role of F18-FDG-PET/CT in restaging patients affected by renal carcinoma.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Bertagna F; Motta F; Bertoli M; Bosio G; Fisogni S; Tardanico R; Ferrari V; Antonelli A; Simeone C; Cosciani Cunico S; Giubbini R

**INSTITUCIÓN / INSTITUTION:** francesco.bertagna@med.unibs.it.

**RESUMEN / SUMMARY:** BACKGROUND: Renal cancers account for around 3% of all cancers and the most common type of (90%) is renal cell carcinoma. Five-year survival rate in renal cancer patients is 68.4%. AIM: The aim of our study was to establish the role of F18-FDG-PET/CT in restaging patients with renal carcinoma who underwent partial or radical nephrectomy. Secondary aim of the study was to identify histological characteristics of the primary tumour that may be responsible for the metabolic behaviour of neoplastic lesions. MATERIALS AND METHODS: We retrospectively evaluated 68 patients with renal carcinoma in whom F18-FDG-PET/CT was performed. RESULTS: Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of F18-FDG PET/CT were 82%, 100%, 100%, 66.7% and 86.8%, respectively. CONCLUSIONS: The results of our study suggest that F18-FDG PET/CT is characterised by high specificity and positive predictive value and can be useful in restaging patients affected by renal carcinoma. However, due to low negative predictive value, this method cannot be recommended for definitely ruling out suspected disease relapse.

[1105]
**TÍTULO / TITLE:** Knockdown of clusterin inhibits the growth and migration of renal carcinoma cells and leads to differential gene expression.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Shi H; Deng JH; Wang Z; Cao KY; Zhou L; Wan H

**INSTITUCIÓN / INSTITUTION:** Department of Urology, The First People’s Hospital Affiliated to Guangzhou Medical University, Guangzhou 510180, P.R. China.

**RESUMEN / SUMMARY:** Clusterin (CLU) is a glycoprotein involved in tumor progression, whose expression level correlates with the metastasis of renal cell carcinoma (RCC). However, the mechanism by which CLU plays an oncogenic
role in RCC remains unclear. In this study, we used the human renal cancer cell 786-O as an experimental model. We knocked down CLU expression in the 786-O cells using lentiviral vector-mediated delivery of RNAi, and then compared the gene expression profiles between the knocked down CLU 786-O cells and control cells. We observed that CLU knockdown induced apoptosis and inhibited the proliferation and migration of 786-O cells. Microassay analysis revealed changes in the expression of 588 genes between the 786-O cells infected by a si-CLU lentivirus and the control cells, where 356 genes were upregulated and 232 were downregulated. Pathway analysis classified the differentially expressed genes into 17 upregulated and 12 downregulated pathways, including the PI3K/Akt, MAPK and VEGF pathways. In this study, we demonstrated that CLU acts as an oncogene in RCC by promoting cell proliferation and migration and inhibiting apoptosis. Microassay analysis may provide a platform for further characterization of the individual genes implicated in the development of RCC, providing new insights into the oncogenic role of CLU.

[1106]
TÍTULO / TITLE: - Constitutively active androgen receptor variants upregulate expression of mesenchymal markers in prostate cancer cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Cottard F; Asmane I; Erdmann E; Bergerat JP; Kurtz JE; Ceraline J
INSTITUCION / INSTITUTION: - INSERM U1113, Federation de Medecine Translationnelle de Strasbourg (FMTS), Universite de Strasbourg, Strasbourg, France.
RESUMEN / SUMMARY: - Androgen receptor (AR) signaling pathway remains the foremost target of novel therapeutics for castration-resistant prostate cancer (CRPC). However, the expression of constitutively active AR variants lacking the carboxy-terminal region in CRPC may lead to therapy inefficacy. These AR variants are supposed to support PCA cell growth in an androgen-depleted environment, but their mode of action still remains unresolved. Moreover, recent studies indicate that constitutively active AR variants are expressed in primary prostate tumors and may contribute to tumor progression. The aim of this study was to investigate the impact of constitutively active AR variants on the expression of tumor progression markers. N-cadherin expression was analyzed in LNCaP cells overexpressing the wild type AR or a constitutively active AR variant by qRT-PCR, Western blot and immunofluorescence. We showed here for the first time that N-cadherin expression was increased in the presence of
constitutively active AR variants. These results were confirmed in C4-2B cells overexpressing these AR variants. Although N-cadherin expression is often associated with a downregulation of E-cadherin, this phenomenon was not observed in our model. Nevertheless, in addition to the increased expression of N-cadherin, an upregulation of other mesenchymal markers expression such as VIMENTIN, SNAIL and ZEB1 was observed in the presence of constitutively active variants. In conclusion, our findings highlight novel consequences of constitutively active AR variants on the regulation of mesenchymal markers in prostate cancer.

[1107]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

- Enlace al texto completo (gratuito o de pago) 5489/cuaj.502

AUTORES / AUTHORS: - Klinghoffer Z; Tarride JE; Novara G; Ficarra V; Kapoor A; Shayegan B; Braga LH
INSTITUCIÓN / INSTITUTION: - Division of Urology, McMaster University, Hamilton, ON;

RESUMEN / SUMMARY: - OBJECTIVES: We compare the cost-utility of laparoscopic radical nephrectomy (LRN), laparoscopic partial nephrectomy (LPN) and open partial nephrectomy (OPN) in the management of small renal masses (SRMs) when the impact of ensuing chronic kidney disease (CKD) disease is considered. METHODS: We designed a Markov decision analysis model with a 10-year time horizon. Estimates of costs, utilities, complication rates and probabilities of developing CKD were derived from the literature. The base case patient was assumed to be a 65-year-old patient with a <4-cm unilateral renal mass, a normal contralateral kidney and a normal preoperative serum creatinine. Univariate and probabilistic sensitivity analyses were conducted to address the uncertainty associated with the study parameters. RESULTS: OPN was the least costly strategy at $25 941 USD and generated 7.161 quality-adjusted life years (QALYs) over 10 years. LPN yielded 0.098 additional QALYs at an additional cost of $888 for an incremental cost-effectiveness ratio of $9057 per QALY, well below a commonly cited willingness-to-pay threshold of $50 000 per QALY. LRN was more costly and yielded fewer QALYs than OPN and LPN. Sensitivity analyses demonstrated our model to be robust to changes to key parameters. Age had no effect on preferred strategy. CONCLUSIONS: Partial nephrectomy (PN) is the preferred treatment strategy for SRMs. In centres where LPN is not available, OPN remains considerably more cost-effective than LRN. Furthermore, our study...
demonstrates that there is no age at which PN is not preferred to LRN. Our study provides additional evidence to advocate PN for the management of all amenable SRMs.

[1108]
**TÍTULO / TITLE:** - Microvesicles derived from human umbilical cord Wharton’s jelly mesenchymal stem cells attenuate bladder tumor cell growth in vitro and in vivo.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago)
1371/journal.pone.0061366

**AUTORES / AUTHORS:** - Wu S; Ju GQ; Du T; Zhu YJ; Liu GH

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Shanghai First People’s Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China ; Department of Urology, Qingdao Municipal Hospital, Qingdao, Shandong, China.

**RESUMEN / SUMMARY:** - Several studies suggest that mesenchymal stem cells (MSCs) possess antitumor properties; however, the exact mechanisms remain unclear. Recently, microvesicles (MVs) are considered as a novel avenue intercellular communication, which may be a mediator in MSCs-related antitumor effect. In the present study, we evaluated whether MVs derived from human umbilical cord Wharton’s jelly mesenchymal stem cells (hWJMSCs) may inhibit bladder tumor T24 cells growth using cell culture and the BALB/c nu/nu mice xenograft model. CCK-8 assay and Ki-67 immunostaining were performed to estimate cell proliferation in vitro and in vivo. Flow cytometry and TUNEL assay were used to assess cell cycle and apoptosis. To study the conceivable mechanism by which hWJMSC-MVs attenuate bladder tumor T24 cells, we estimated the expression of Akt/p-Akt, p-p53, p21 and cleaved Caspase 3 by Western blot technique after exposing T24 cells to hWJMSC-MVs for 24, 48 and 72h. Our data indicated that hWJMSC-MVs can inhibit T24 cells proliferative viability via cell cycle arrest and induce apoptosis in T24 cells in vitro and in vivo. This study showed that hWJMSC-MVs down-regulated phosphorylation of Akt protein kinase and up-regulated cleaved Caspase 3 during the process of anti-proliferation and pro-apoptosis in T24 cells. These results demonstrate that hWJMSC-MVs play a vital role in hWJMSC-induced antitumor effect and may be a novel tool for cancer therapy as a new mechanism of cell-to-cell communication.

[1109]
**TÍTULO / TITLE:** - Stereotactic body radiotherapy for localized prostate cancer: disease control and quality of life at 6 years.

809
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

Enlace al texto completo (gratuito o de pago) 1186/1748-717X-8-118

AUTORES / AUTHORS: - Katz AJ; Santoro M; Diblasio F; Ashley R

RESUMEN / SUMMARY: - BACKGROUND: Stereotactic body radiotherapy (SBRT) may yield disease control for prostate cancer in a brief, hypofractionated treatment regimen without increasing treatment toxicity. Our report presents a 6-year update from 304 low- (n = 211), intermediate- (n = 81), and high-risk (n = 12) prostate cancer patients who received CyberKnife SBRT. METHODS: The median PSA at presentation was 5.8 ng/ml. Fifty-seven patients received neoadjuvant hormonal therapy for up to one year. The first 50 patients received a total dose of 35 Gy in 5 fractions of 7 Gy. The subsequent 254 patients received a total dose of 36.25 Gy in 5 fractions of 7.25 Gy. Toxicity was assessed with the Expanded Prostate Cancer Index Composite questionnaire and the Radiation Therapy Oncology Group urinary and rectal toxicity scale. Biochemical failure was assessed using the nadir + 2 definition. RESULTS: No patients experienced Grade III or IV acute complications. Fewer than 5% of patients experienced any acute Grade II urinary or rectal toxicities. Late urinary Grade II complications were observed in 4% of patients treated to 35 Gy and 9% of patients treated to 36.25 Gy. Five (2%) late Grade III urinary toxicities occurred in patients who were treated with 36.25 Gy. Late Grade II rectal complications were observed in 2% of patients treated to 35 Gy and 5% of patients treated to 36.25 Gy. Bowel and urinary quality of life (QOL) scores initially decreased, but later returned to baseline values. An overall decrease of 20% in the sexual QOL score was observed. QOL in each domain was not differentially affected by dose. For patients that were potent prior to treatment, 75% stated that they remained sexually potent. Actuarial 5-year biochemical recurrence-free survival was 97% for low-risk, 90.7% for intermediate-risk, and 74.1% for high-risk patients. PSA fell to a median of 0.12 ng/ml at 5 years; dose did not influence median PSA levels. CONCLUSIONS: In this large series with long-term follow-up, we found excellent biochemical control rates and low and acceptable toxicity, outcomes consistent with those reported for from high dose rate brachytherapy (HDR BT). Provided that measures are taken to account for prostate motion, SBRT’s distinct advantages over HDR BT include its noninvasiveness and delivery to patients without anesthesia or hospitalization.

[1110]

TÍTULO / TITLE: - Action Mechanism of Ginkgo biloba Leaf Extract Intervened by Exercise Therapy in Treatment of Benign Prostate Hyperplasia.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Evid Based Complement Alternat Med.


Enlace al texto completo (gratuito o de pago) 1155/2013/408734

810
RESUMEN / SUMMARY: Benign prostatic hyperplasia (BPH), an imbalance between androgen/estrogen, overexpression of stromal, and epithelial growth factors associated with chronic inflammation, has become an atypical direct cause of mortality of aged male diseases. Ginkgo possesses anti-inflammatory, blood flow-enhancing, and free radical scavenging effects. Considering strenuous exercise can reduce BPH risks, we hypothesize Ginkgo + exercise (Ginkgo + Ex) could be beneficial to BPH. To verify this, rat BPH model was induced by s.c. 3.5 mg testosterone (T) and 0.1 mg estradiol (E2) per head per day successively for 8 weeks, using mineral oil as placebo. Cerenin® 8.33 μL/100 g was applied s.c. from the 10th to the 13th week, and simultaneously, Ex was applied (30 m/min, 3 times/week). In BPH, Ginkgo alone had no effect on T, 5 alpha-reductase, and dihydrotestosterone (DHT), but suppressed androgen receptor (AR), aromatase, E2 and estrogen receptor (ER), and the proliferating cell nuclear antigen (PCNA); Ex alone significantly reduced T, aromatase, E2, ER, AR, and PCNA, but highly raised DHT. While Ginkgo + Ex androgenically downregulated T, aromatase, E2, and ER, but upregulated DHT, AR, and PCNA, implying Ginkgo + Ex tended to worsen BPH. Conclusively, Ginkgo or Ex alone may be more beneficial than Ginkgo + Ex for treatment of BPH.
immunotherapy, radiopharmaceuticals and bone-targeted agents. The recent improvement in prognosis for CRPC brings continued optimism for further improvements. Thoughtful planning of clinical trials and further understanding of the mechanisms of resistance to therapies will allow for continued progress in patient care.

[1112]
TÍTULO / TITLE: - Targeting psychoemotional stress to treat prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kulik G

[1113]
TÍTULO / TITLE: - Possible Relation between the NOS3 Gene GLU298ASP Polymorphism and Bladder Cancer in Turkey.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Verim L; Toptas B; Ozkan NE; Cacina C; Turan S; Korkmaz G; Yaylim I
INSTITUCIÓN / INSTITUTION: - Haydarpasa Numune Training Hospital, Urology Department, Istanbul, Turkey E-mail: ilhanyaylim@gmail.com.
RESUMEN / SUMMARY: - Endothelial nitric oxide synthase (eNOS), encoded by the NOS3 gene, has been suggested to play an important role in uncontrolled cell growth in several cancer types. The objective of this study was to evaluate the role of the NOS3 Glu298Asp polymorphism in bladder cancer susceptibility in a Turkish population. We determined the genotypes of 66 bladder cancer cases and 88 healthy controls. Genotypes were determined by polymerase chain reaction-restriction fragment length polymorphism analysis. A significant association for NOS3 Glu298Asp heterozygotes genotypes and T allele were found between healthy controls and bladder cancer, respectively (p<0.001: p=0.002). There were no significant associations between any genotypes and the stage, grade, and histological type of bladder cancer. Our study suggested an increased risk role of NOS3 GT genotype in bladder cancer susceptibility in our Turkish population.
Identification of comorbidities that place men at highest risk of death from androgen deprivation therapy before brachytherapy for prostate cancer.

Parekh A; Chen MH; D'Amico AV; Dosoretz DE; Ross R; Salenius S; Graham PL; Beckman JA; Beard CJ; Choueiri TK; Ennis RD; Hoffman KE; Hu JC; Ma J; Martin NE; Nguyen PL

Department of Radiation Oncology, Dana Farber/Brigham and Women’s Hospital, Harvard Medical School, Boston, MA.

PURPOSE: To determine which specific comorbidities predispose men to excess mortality by androgen deprivation therapy (ADT) given before and during brachytherapy for prostate cancer. METHODS AND MATERIALS: We analyzed 5972 men with T1c-T3b prostate cancer treated with brachytherapy-based radiation with or without neoadjuvant ADT. Cox multivariable analysis with propensity scoring was used to determine if ADT was associated with increased all-cause mortality (ACM) in men divided into groups stratified by cardiac comorbidities. Tests for interaction between risk group and outcome were performed. RESULTS: ADT was associated with increased ACM in men with a history of congestive heart failure or myocardial infarction, regardless of whether they were revascularized (adjusted hazard ratio [AHR], 2.1 [95% confidence interval {CI}, 1.02-4.17; p=0.04]) or not (AHR, 1.8 [95% CI, 1.05-3.20; p = 0.03]), but this effect was not seen in men with less severe comorbidity. However, among men with diabetes, there was a significant interaction with risk group (p=0.01) such that ADT was associated with excess mortality in men with low-risk disease (AHR = 2.21 [1.04-4.68]; p=0.04) but not in men with intermediate or high-risk disease (AHR, 0.64 [0.33-1.22]; p=0.17). CONCLUSIONS: ADT was associated with excess ACM in all patients with a history of congestive heart failure or myocardial infarction, regardless of whether they were revascularized, and in diabetics with low-risk disease. ADT for gland downsizing before brachytherapy should be avoided in these men.

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Expression analysis of RNA-binding motif gene on Y chromosome (RBMY) protein isoforms in testis tissue and a testicular germ cell cancer-derived cell line (NT2).

Alikhani M; Sharifi Tabar M; Mirshahvaladi S; Kheimeh A; Sadighi Gilani MA; Sabbaghian M

INSTITUCIÓN / INSTITUTION: - Dept. of Andrology at Reproductive Biomedicine Research Center, Royan Institute, ACECR, Tehran, Iran.

RESUMEN / SUMMARY: - BACKGOUND: RNA-binding motif gene on Y chromosome (RBMY), a germ cell-specific nuclear protein, is known as a key factor in spermatogenesis and disorders associated with this protein have been recognized to be related to male infertility. Although it was suggested that this protein could have different functions during germ cell development, no studies have been conducted to uncover the mechanism of this potential function yet. Here, we analyzed the expression pattern of RBMY protein isoforms in testis compared to NT2, a testicular germ cell cancer-derived cell line, to test probability of differential expression of RBMY protein isoforms at different spermatogenesis stages. METHODS: Full length and a segment of RBMY gene were cloned and expressed in E. coli. Anti-human RBMY antibody was produced in rabbit using the recombinant proteins as antigen. Western-blot and immunofluorescence were conducted for detection and comparison of RBMY protein isoforms. RESULTS: Selected segment of RBMY protein resulted in producing a mono-specific antibody. As results shows, only the longest isoform of RBMY was expressed at protein level in NT2 cell line, while three isoforms of this protein were detected in the whole testis lysate. CONCLUSION: The results imply that different alternative splicing may happen in testis cells and probably difference of RBMY function during spermatogenesis is due to the differential expression of RBMY protein isoforms. These results and further experiments on RBMY isoforms can help to obtain a better understanding of the function of this protein, which may increase our knowledge about spermatogenesis and causes of male infertility.

TÍTULO / TITLE: - Androgen receptor decreases the cytotoxic effects of chemotherapeutic drugs in upper urinary tract urothelial carcinoma cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hsieh TF; Chen CC; Yu AL; Ma WL; Zhang C; Shyr CR; Chang C

INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Surgery, Buddhist Tzu Chi General Hospital, Taichung Branch, Taichung 40427;

RESUMEN / SUMMARY: - Upper urinary tract urothelial carcinomas (UUTUCs) represent relatively uncommon yet devastating tumors that affect more males than females. However, the correlation between gender difference and disease progression remains unclear. Androgen and the androgen receptor (AR) were previously hypothesized to account for the gender difference in the incidence of urothelial carcinomas; however, the role of AR in the development and progression of UUTUCs is not well understood. In addition, although UUTUCs
are responsive to chemotherapy, various responses are presented among patients. Therefore, the aim of the present study was to determine the role of AR in the response of UUTUC cells to chemotherapeutic drugs. In this study, AR overexpression in UUTUC cells (BFTC 909) was identified to reduce the cytotoxic effect of chemotherapeutic drugs, including doxorubicin, cisplatin and mitomycin C and protected cells from drug-induced death. The expression of ABCG2, an ATP-binding cassette half-transporter associated with multidrug resistance, was increased in AR-overexpressing BFTC cells. In addition, use of the AR degradation enhancer, ASC-J9®, repressed the AR effect on increasing cell viability under drug treatment. In summary, results of the present study indicate that the status of AR expression levels in UUTUCs may be a significant factor in affecting the efficacy of chemotherapy and classic chemotherapeutic drugs and AR targeted therapy may provide a novel potential therapeutic approach to improve treatment of UUTUCs.

[1117]

TÍTULO / TITLE: - Study of global transcriptional changes of N-GlcNAc2 proteins-producing T24 bladder carcinoma cells under glucose deprivation.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Isono T; Chano T; Okabe H; Suzaki M

INSTITUCIÓN / INSTITUTION: - Central Research Laboratory, Shiga University of Medical Science, Otsu, Shiga, Japan. isono@belle.shiga-med.ac.jp

RESUMEN / SUMMARY: - Increased levels of N-linked (beta-N-acetylglucosamine)2 [N-GlcNAc2]-modified proteins have been recognized to be an effective response to glucose deprivation. In the first step of this study, using a next generation sequencer, we investigated the global transcriptional changes induced by glucose deprivation in a T24 bladder carcinoma cell line, producing N-GlcNAc2-modified proteins under glucose deprivation. Our transcriptome analysis revealed significant up-regulation of the UDP-GlcNAc biosynthesis pathway and unfolded protein response genes, and down-regulation of G2/M transition-related genes containing mitotic kinases. Our biological analysis confirmed that N-GlcNAc2-modified proteins were localized with BiP proteins in the ER. G2/M arrest was caused by glucose deprivation in T24 cells. Moreover, the knockdown of unfolded protein response genes induced the expression recovery of mitotic kinases under glucose deprivation. Taken together, our results suggest N-GlcNAc2-modified proteins produced under glucose deprivation caused unfolded protein response in the ER, and that this response induced G2/M arrest.

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[1118]
**TITULO / TITLE:** - Prostate cancer: Best nomograms for predicting insignificant disease.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.92

[1119]
**TITULO / TITLE:** - Urothelial carcinoma: Everolimus of limited efficacy for metastatic disease.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.90

[1120]
**TITULO / TITLE:** - Sequential treatment strategies and combination therapy regimens in metastatic renal cell carcinoma.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** - Pal SK; Vogelzang NJ
**INSTITUCIÓN / INSTITUTION:** - Department of Medical Oncology & Experimental Therapeutics, City of Hope Comprehensive Cancer Center, Duarte, California 91010, USA. SPal@coh.org
**RESUMEN / SUMMARY:** - Molecularly-targeted therapies have revolutionized the treatment of metastatic renal cell carcinoma (mRCC), but unmet needs remain. Efficacy of targeted agents is transient, and questions regarding optimal sequencing of therapies and benefits versus risks of combination therapy remain largely unanswered. In this article, an overview of ongoing/recently completed clinical trials evaluating sequential treatment strategies and combination therapy regimens is presented, along with a brief discussion of predictive biomarkers and prognostic factors. Several ongoing/recently completed clinical studies have been designed to help address 2 major questions currently facing physicians treating patients with mRCC: 1) What is the optimal sequence of targeted agents? and 2) Does combination therapy with targeted agents benefit patients with mRCC? Results of these trials may help establish the degree to which cross-resistance between agents occurs and which agents, when used consecutively, are associated with the most favorable outcomes. Clinical trial data maturing in the next 1-2 years should provide insight into the most effective treatment sequences and the benefits versus risks of combination therapies. Whether results of these studies will lead to a paradigm shift in treatment recommendations for patients with mRCC remains to be determined.

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816
The study investigated possible mechanisms by which sanguinarine exerts its anticancer action in cultured human bladder cancer cell lines (T24, EJ, and 5637). Sanguinarine treatment resulted in concentration-response growth inhibition of the bladder cancer cells by inducing apoptosis. Sanguinarine-induced apoptosis was correlated with the up-regulation of Bax, the down-regulation of Bid and XIAP, the activation of caspases (-3, -8, and -9), and the generation of increased reactive oxygen species (ROS). The ROS scavenger N-acetyl cysteine (NAC) completely reversed the sanguinarine-triggered apoptotic events. In addition, sanguinarine effectively increased the activation of the c-Jun N-terminal kinase (JNK) and the expression of the early growth response gene-1 (Egr-1), which was recovered by pretreatment with NAC. Furthermore, knockdown of Egr-1 expression by small interfering RNA attenuated sanguinarine-induced apoptosis, but not the JNK inhibitor, indicating that the interception of ROS generation blocked the sanguinarine-induced apoptotic effects via deregulation of the expression of Egr-1 proteins. Taken together, the data provide evidence that sanguinarine is a potent anticancer agent, which inhibits the growth of bladder cancer cells and induces their apoptosis through the generation of free radicals.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Rashid MM; Alam AK; Habib AK; Rahman H; Hossain AK; Salam MA; Rahman S

INSTITUCIÓN / INSTITUTION: - Department of Urology, Bangabandhu Sheikh Mujib Medical University, Dhaka. drmamon21@yahoo.com

RESUMEN / SUMMARY: - Indications of prostate biopsy are high serum prostate specific antigen (PSA) value and or abnormal digital rectal examination (DRE) findings. Although serum PSA value of 4 ng/ml is the most commonly used threshold for recommending prostate biopsy, significant proportion of men harbor prostate cancer even when their serum PSA values are less than 4.0 ng/ml. Therefore present study was designed to determine the performance status of serum PSA in lower cut-off values. This hospital based prospective study was conducted in the Department of Urology of Bangabandhu Sheikh Mujib Medical University (BSMMU) and Comfort Nursing Home Pvt. Ltd, Dhaka from July 2009 to October 2010. Two hundred six male patients aged over 50 years having lower urinary tract symptoms (LUTS) and serum PSA more than 2.5 ng/ml were prepared for prostate biopsy. Trans rectal ultrasound (TRUS) guided biopsy was done. The test statistics used to analyze the data were descriptive statistics, sensitivity, specificity, positive and negative predictive value, ROC curve. For all analytical tests, the level of significance was set at 0.05 and p < 0.05 was considered significant. In 2.5-4 serum PSA range, 28.26% (13 out of 46) of all malignancy were found, which would be missed if we take cut off value 4. At 2.5 PSA cut-off, Sensitivity 91.3%, Specificity 14.37%, PPV 23.46%, NPV 85.18%, Efficacy 31.55%. At 4 PSA cut-off value, Sensitivity 71.73%, Specificity 46.25%, PPV 27.73%, NPV 85.05%, Efficacy 51.94%. So it can be concluded that, for early diagnosis of prostate cancer cut-off value of serum PSA of 2.5 ng/ml can be recommended as an indication for prostate biopsy.

[1123]

TÍTULO / TITLE: - Oxidative stress in prostate cancer: changing research concepts towards a novel paradigm for prevention and therapeutics.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Paschos A; Pandya R; Duivenvoorden WC; Pinthus JH

INSTITUCIÓN / INSTITUTION: - Department of Surgery, McMaster University and Juravinski Cancer Centre, Hamilton, Ontario, Canada.

RESUMEN / SUMMARY: - A mounting body of evidence suggests that increased production of reactive oxygen species (ROS) is linked to aging processes and to the etiopathogenesis of aging-related diseases, such as cancer, diabetes, atherosclerosis and degenerative diseases like Parkinson’s and Alzheimer’s.
Excess ROS are deleterious to normal cells, while in cancer cells, they can lead to accelerated tumorigenesis. In prostate cancer (PC), oxidative stress, an innate key event characterized by supraphysiological ROS concentrations, has been identified as one of the hallmarks of the aggressive disease phenotype. Specifically, oxidative stress is associated with PC development, progression and the response to therapy. Nevertheless, a thorough understanding of the relationships between oxidative stress, redox homeostasis and the activation of proliferation and survival pathways in healthy and malignant prostate remains elusive. Moreover, the failure of chemoprevention strategies targeting oxidative stress reduced the level of interest in the field after the recent negative results of the Selenium and Vitamin E Cancer Prevention Trial (SELECT) trial. Therefore, a revisit of the concept is warranted and several key issues need to be addressed: The consequences of changes in ROS levels with respect to altered redox homeostasis and redox-regulated processes in PC need to be established. Similarly, the key molecular events that cause changes in the generation of ROS in PC and the role for therapeutic strategies aimed at ameliorating oxidative stress need to be identified. Moreover, the issues whether genetic/epigenetic susceptibility for oxidative stress-induced prostatic carcinogenesis is an individual phenomenon and what measurements adequately quantify prostatic oxidative stress are also crucial. Addressing these matters will provide a more rational basis to improve the design of redox-related clinical trials in PC. This review summarizes accepted concepts and principles in redox research, and explores their implications and limitations in PC. Prostate Cancer and Prostatic Disease advance online publication, 14 May 2013; doi:10.1038/pcan.2013.13.

[1124]
TÍTULO / TITLE: - Prostatic Adenocarcinoma Masquerading as Generalized lymphadenopathy and Mimicking lymphoma on FDG PET/CT: Diagnosis, Staging, and Evaluation of Therapy Response by FDG PET/CT.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Joshi P; Lele V
INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine and PET-CT, Jaslok Hospital and Research Centre, Mumbai, India.
RESUMEN / SUMMARY: - We report a case of prostatic adenocarcinoma, initially presenting with generalized lymphadenopathy, and mimicking lymphoma on fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT). Our case suggests that in elderly men presenting with generalized lymphadenopathy, the diagnosis of metastatic prostatic carcinoma should not be overlooked even in the absence of typical urinary symptoms. The
establishment of a diagnosis of metastatic prostate carcinoma is important, because even widespread prostate cancer may be responsive to hormonal treatment, as demonstrated by this case. We also describe the use of FDG PET/CT to diagnose, stage, and evaluate response to hormonal treatment in a given patient.

[1125]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Lombrana M; Izquierdo L; Gomez A; Alcaraz A

INSTITUCIÓN / INSTITUTION: - Maria Lombrana, MN, RN, Department of Urology, Hospital Clinic, Barcelona, España. Laura Izquierdo, MD, PhD, Department of Urology, Hospital Clinic, Barcelona, España. Ascension Gomez, RN, Department of Urology, Hospital Clinic, Barcelona, España Antonio Alcaraz, MD, PhD, Department of Urology, Hospital Clinic, Barcelona, España.

RESUMEN / SUMMARY: - PURPOSE: : To determine the prevalence of urinary incontinence (UI) in patients undergoing prostatectomy and to evaluate the impact of UI on the everyday life in order to select the patients eligible to enter a pelvic floor rehabilitation program. SUBJECTS AND SETTINGS: : The sample comprised 114 consecutive men undergoing laparoscopic or open radical prostatectomy between April 2007 and April 2008. Participants’ mean age was 59 years (range, 46-67 years). The research setting was a hospital-based clinic in Barcelona, España. Patients who required an indwelling urinary catheter due to other factors were excluded from the trial. During admission, nursing staff explained the study and obtained informed consent from patients willing to participate in the trial. METHODS: : The impact of UI on daily living was evaluated via administration of the International Consultation on Incontinence Questionnaire-Short Form. Impact of UI was evaluated before surgery, and after 1 and 12 months following indwelling catheter removal. RESULTS: : A total of 95.5% patients developed UI 1 month following bladder catheter removal. Slightly less than 1 in 4 patients (24.8%) indicated that UI had no effect on activities of daily living. In contrast, 27.5% indicated that UI had a moderate impact and 47.7% indicated a severe impact. Ninety-one patients reported performing pelvic floor muscle exercises to improve UI, but only 45% were found to be performing them correctly. When evaluated at 1 year following catheter removal, 52.64% of the patients continued to experience UI. The majority (79.8%) indicated that UI did not impact their daily lives, 8.8% indicated a moderate impact, and 20.4% reported that UI had a severe impact on daily
Seventy patients (61.4%) continued to perform pelvic floor muscle exercises; after 1 year, 93% were deemed to be correctly identifying, contracting, and relaxing their pelvic floor muscles. CONCLUSIONS: Urinary incontinence remains prevalent as long as 12 months following catheter removal. Incontinence exerts a moderate to severe impact on daily life in 27.5% to 20.4% of respondents. In order to minimize the negative impact as much as possible, we advocate a pelvic floor muscle training program overseen by RNs.

[1126]

**TITULO / TITLE:** Kidney cancer and diabetes mellitus: a population-based case-control study in Taiwan.
**RESUMEN / SUMMARY:** [Enlace al Resumen / Link to its Summary]
**AUORES / AUTHORS:** Lai SW; Liao KF; Lai HC; Tsai PY; Sung FC; Chen PC
**INSTITUCIÓN / INSTITUTION:** School of Medicine, China Medical University, Taichung, 404, Taiwan.
**RESUMEN / SUMMARY:** INTRODUCTION: The purpose of this study was to explore whether diabetes mellitus (DM) correlates with the risk of kidney cancer in Taiwan. MATERIALS AND METHODS: We designed a population-based case-control study from the Taiwan National Health Insurance Database, which consisted of 116 patients with newly diagnosed kidney cancer as cases and 464 subjects without kidney cancer as controls in 2000 to 2009. Both cases and controls were aged >/=20 years. Baseline comorbidities were compared between kidney cancer cases and controls. RESULTS: Multivariable analysis showed no association was detected between DM and kidney cancer (OR 1.06, 95% CI, 0.58 to 1.94). Hypertension (OR 2.05, 95% CI, 1.23 to 3.42), chronic kidney diseases (OR 2.57, 95% CI, 1.23 to 5.37), cystic kidney diseases (OR 18.6, 95% CI, 1.84 to 187.6) and kidney stones (OR 4.02, 95% CI, 2.43 to 6.66) were significant comorbidities associated with increased risk of kidney cancer. Use of alpha-glucosidase inhibitor was associated with increased risk of kidney cancer (OR 4.31, 95% CI, 1.07 to 17.3). CONCLUSION: DM does not correlate with the risk of kidney cancer. Hypertension, chronic kidney diseases, cystic kidney diseases, kidney stones and use of alpha-glucosidase inhibitors are associated with kidney cancer.

[1127]

**TITULO / TITLE:** Expression and purification of recombinant proteins based on human prostate stem cell antigen and heat shock protein-70.
**RESUMEN / SUMMARY:** [Enlace al Resumen / Link to its Summary]
The aim of this study was to express and purify recombinant proteins based on human prostate stem cell antigen (PSCA) and heat shock protein-70 (HSP70). The PSCA gene and various structural domains of HSP70 were amplified by polymerase chain reaction (PCR) with the respective primers. Then, the PSCA was cloned into the prokaryotic expression vector pET21a(+) with the amino-terminus, carboxyl-terminus and overall length of HSP70, by enzyme digestion to construct the recombinant plasmids pET21-PSCA-HSPC and pET21-PSCA-HSP, respectively. After being expressed in Escherichia coli (E. coli) by isopropyl beta-D-1-thiogalactopyranoside (IPTG) induction, recombinant fusion proteins were purified. Western blotting was performed to confirm the expression of the recombinant proteins. The results revealed that recombinant plasmids were successfully constructed. The PSCA-HSPC and PSCA-HSP expressed in E. coli existed in soluble form, as confirmed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). The purity of the recombinant proteins PSCA-HSPC and PSCA-HSP reached >95% following purification with the nickel-nitrilotriacetic acid (Ni-NTA) resin, Phenyl-Sepharose Fast Flow and Superdex 75, which lays a foundation for the development of vaccines for prostate cancer.

[1128]

Vascular endothelial growth factor (VEGF) expression in locally advanced prostate cancer: secondary analysis of radiation therapy oncology group (RTOG) 8610.

BACKGROUND: Angiogenesis is a key element in solid-tumor growth, invasion, and metastasis. VEGF is among the most potent angiogenic factor thus far detected. The aim of the present study is to explore the potential of VEGF (also known as VEGF-A) as a prognostic and predictive biomarker among men with locally advanced prostate cancer. METHODS: The
analysis was performed using patients enrolled on RTOG 8610, a phase III randomized control trial of radiation therapy alone (Arm 1) versus short-term neoadjuvant and concurrent androgen deprivation and radiation therapy (Arm 2) in men with locally advanced prostate carcinoma. Tissue samples were obtained from the RTOG tissue repository. Hematoxylin and eosin slides were reviewed, and paraffin blocks were immunohistochemically stained for VEGF expression and graded by Intensity score (0-3). Cox or Fine and Gray’s proportional hazards models were used. RESULTS: Sufficient pathologic material was available from 103 (23%) of the 456 analyzable patients enrolled in the RTOG 8610 study. There were no statistically significant differences in the pre-treatment characteristics between the patient groups with and without VEGF intensity data. Median follow-up for all surviving patients with VEGF intensity data is 12.2 years. Univariate and multivariate analyses demonstrated no statistically significant correlation between the intensity of VEGF expression and overall survival, distant metastasis, local progression, disease-free survival, or biochemical failure. VEGF expression was also not statistically significantly associated with any of the endpoints when analyzed by treatment arm. CONCLUSIONS: This study revealed no statistically significant prognostic or predictive value of VEGF expression for locally advanced prostate cancer. This analysis is among one of the largest sample bases with long-term follow-up in a well-characterized patient population. There is an urgent need to establish multidisciplinary initiatives for coordinating further research in the area of human prostate cancer biomarkers.

[1129]
TITULO / TITLE: - Prevention and Detection of Prostate Cancer: A Pilot Intervention in a Resource-Poor South African Community.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Matshela RF; Maree JE; van Belkum C
INSTITUCION / INSTITUTION: - Author affiliations: Adelaide Tambo School of Nursing Science, Tshwane University of Technology, Pretoria (Mr Matshela and Dr van Belkum); Department of Nursing Education, University of the Witwatersrand, Johannesburg, South Africa (Dr Maree).

RESUMEN / SUMMARY: - BACKGROUND:: Prostate cancer is a global health problem strongly linked to the Western lifestyle and its health risks. South Africa, like many African countries, has no population-based screening for this disease. OBJECTIVE:: The purpose of this study was to develop and pilot test an intervention focused on the prevention and detection of prostate cancer in a resource-poor community in Tshwane, South Africa. INTERVENTION:: Personal invitations for screening were extended to 122 men 40 years or older.
Those presenting for screening received health education on prostate cancer and were screened using digital rectal examination and a prostate-specific antigen (PSA) test. Follow-up appointments were also arranged. RESULTS:: Only 53.3% (n = 65) of the invitees reported for screening, with 38 (58.5%) returning to the clinic to learn the results of the PSA test. Knowledge of prostate cancer improved significantly after the intervention. Abnormal findings were detected in 6.2% (n = 4) of the participants, and elevations in PSA levels, in 12.3% (n = 8). CONCLUSIONS:: Disappointing results in terms of screening uptake and the number of men lost to follow-up were achieved. The strategies to improve knowledge were successful and resulted in a significant increase in knowledge of prostate cancer. IMPLICATIONS FOR NURSING PRACTICE:: The success of a cancer prevention and detection service is determined by participation and screening uptake. The reasons for not accepting the screening invitation and not returning to learn the findings of the PSA test should be explored. Preventative strategies should be developed and tested as part of a second pilot study testing the refined intervention.

[1130]
TITULO / TITLE: - Phenethyl isothiocyanate inhibits androgen receptor-regulated transcriptional activity in prostate cancer cells through suppressing PCAF.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Yu C; Gong AY; Chen D; Solelo Leon D; Young CY; Chen XM
INSTITUCION / INSTITUTION: - Department of Medical Microbiology and Immunology, Creighton University Medical Center, Omaha, NE, USA; Department of Clinical Nursing, School of Nursing, Beijing University of Chinese Medicine, Beijing, P. R. China.
RESUMEN / SUMMARY: - SCOPE: Androgen receptor (AR) signaling is critical for all aspects of prostate growth and tumorigenesis. The glucosinolate-derived phenethyl isothiocyanate (PEITC) has recently been demonstrated to reduce the risk of prostate cancer (PCa) and inhibit PCa cell growth. We previously reported that p300/CREB-binding protein-associated factor (PCAF), a co-regulator for AR, is upregulated in PCa cells through suppression of the mir-17 gene. Here, we assessed the effects of PEITC on PCAF expression and AR-regulated transcriptional activity in PCa cells. METHODS AND RESULTS: Using AR-responsive LNCaP cells, we observed the inhibitory effects of PEITC on the dihydrotestosterone-stimulated AR transcriptional activity and cell growth of PCa cells. Interestingly, overexpression of PCAF attenuated the inhibitory effects of PEITC on dihydrotestosterone-stimulated AR transcriptional activity.
Expression of PCAF was upregulated in PCa cells through suppression of miR-17. PEITC treatment significantly decreased PCAF expression and promoted transcription of miR-17 in LNCaP cells. Functional inhibition of miR-17 attenuated the suppression of PCAF in cells treated by PEITC. CONCLUSION: Our results indicate that PEITC inhibits AR-regulated transcriptional activity and cell growth of PCa cells through miR-17-mediated suppression of PCAF, suggesting a new mechanism by which PEITC modulates PCa cell growth.

[1131]

TITULO / TITLE: - Genetics and genomics of prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Dean M; Lou H
INSTITUCIÓN / INSTITUTION: - Cancer and Inflammation Program, National Cancer Institute, National Institutes of Health, Frederick, MD 21702, USA.
RESUMEN / SUMMARY: - Prostate cancer (PCa) is one of the most common malignancies in the world with over 890 000 cases and over 258 000 deaths worldwide each year. Nearly all mortalities from PCa are due to metastatic disease, typically through tumors that evolve to be hormone-refractory or castrate-resistant. Despite intensive epidemiological study, there are few known environmental risk factors, and age and family history are the major determinants. However, there is extreme heterogeneity in PCa incidence worldwide, suggesting that major determining factors have not been described. Genome-wide association studies have been performed and a considerable number of significant, but low-risk loci have been identified. In addition, several groups have analyzed PCa by determination of genomic copy number, fusion gene generation and targeted resequencing of candidate genes, as well as exome and whole genome sequencing. These initial studies have examined both primary and metastatic tumors as well as murine xenografts and identified somatic alterations in TP53 and other potential driver genes, and the disturbance of androgen response and cell cycle pathways. It is hoped that continued characterization of risk factors as well as gene mutation and misregulation in tumors will aid in understanding, diagnosing and better treating PCa.

[1132]

TITULO / TITLE: - Clinical Significance of Wnt/beta-Catenin Signalling and Androgen Receptor Expression in Prostate Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
PURPOSE: To investigate the relationships among the Wnt/beta-catenin pathway, androgen receptor (AR), and clinicopathological factors in hormone-naive prostate cancer.

MATERIALS AND METHODS: This study was conducted with 132 cases of hormone-naive prostate cancer treated by prostatectomy and prostate needle biopsy. An immunohistochemical study using antibodies against beta-catenin, matrix metalloproteinase-7 (MMP-7), and the AR was performed. For the in vitro study, PC-3, LNCaP, 22Rv1, and DU145 cell lines were used. RESULTS: The clinical or pathological stage were a localized cancer in 36 patients (27.3%), locally advanced cancer in 31 (23.5%), and metastatic cancer in 65 (49.2%). We detected increased beta-catenin, AR, and MMP-7 expression with a high Gleason grade, disease progression, and increasing serum prostate-specific antigen (PSA) levels (p<0.01). In Spearman’s rank correlations, the expression of cytoplasmic beta-catenin, MMP-7, and the AR were found to be significantly positively correlated. In addition, the expression of beta-catenin, MMP-7, and the AR were significantly correlated with clinicopathological variables indicative of a poor prognosis. Forty-nine patients with primary androgen deprivation had short response durations from hormone therapy to PSA progression with elevated MMP-7 expression on the Kaplan-Meier curve (p=0.0036). CONCLUSIONS: These data show that an activated Wnt/beta-catenin pathway and AR expression in prostate cancer are correlated with metastasis and aggressiveness. In addition, the expression of MMP-7 protein, a target of the Wnt/beta-catenin pathway, is associated with PSA progression in prostate cancer patients undergoing primary hormone therapy.

[1133]

TÍTULO / TITLE: - Orphan nuclear receptor nurr1 as a potential novel marker for progression in human prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Wang J; Yang J; Zou Y; Huang GL; He ZW

INSTITUCIÓN / INSTITUTION: - Sino-American Cancer Research Institute, Key Laboratory for Medical Molecular Diagnostics of Guangdong Province, Guangdong Medical College, Dongguan, China E-mail: zhiweihe66832@yahoo.cn.
RESUMEN / SUMMARY: - A number of studies have indicated that Nurr1, which belongs to a novel class of orphan nuclear receptors (the NR4A family), is important for carcinogenesis. Here we investigated expression of Nurr1 protein in benign and malignant human prostate tissues and association with clinicopathologic features using immunohistochemical techniques. Moreover, we also investigated the ability of Nurr1 to influence proliferation, migration, invasion and apoptosis of human prostate cancer cells using small interfering RNA silencing. Immunohistochemical analysis revealed that the expression of Nurr1 protein was higher in prostate cancer tissues than in benign prostate tissue (P < 0.001), levels being positively correlated with tumor T classification (P = 0.003), N classification (P = 0.017), M classification (P = 0.011) and the Gleason score (P = 0.020) of prostate cancer patients. In vitro, silencing of endogenous Nurr1 attenuated cell proliferation, migration and invasion, and induced apoptosis of prostate cancer cells. These results suggest that Nurr1 may be used as an indicator for prostate cancer progression and be useful for novel potential therapeutic strategies.

[1134]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ojewola RW; Tijani KH; Jeje EA; Ogunjimi MA; Anunobi CC; Adesanya AO

INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Surgery, Lagos University Teaching Hospital, P.M.B 12003, Lagos.

RESUMEN / SUMMARY: - OBJECTIVE: To evaluate the usefulness of prostate specific antigen (PSA) and digital rectal examination (DRE) in the diagnosis of cancer of the prostate (CaP) amongst unscreened patients. PATIENTS, MATERIALS AND METHODS: A prospective study168 unscreened men who were referred for evaluation for CaP. They all had a 10-core extended transrectal prostatic needle biopsy using size 16 Tru Cut needle for either an elevated serum total PSA of >4ng/ml or abnormal DRE findings or both. Overall cancer detection rate was determined and detection rates were determined separately for patients with elevated PSA with normal DRE, abnormal DRE with normal PSA and those with both indications. The performances of each indication were determined separately and in combination in terms of their sensitivity, specificity, predictive values and accuracy. The results were compared amongst patients with different indications for biopsy. RESULTS: The overall cancer detection rate was 44.0%. Detection rates in patients with elevated PSA with normal DRE and abnormal DRE with normal PSA were
30.0% and 17.4% respectively. There was statistically significant increased detection of 61.2% amongst patients with both indications. The overall sensitivities of PSA, DRE and combination of both were 94.6%, 75.7% and 70.3% respectively while the specificities were 20.2%, 44.7% and 64.9% respectively. The accuracies of PSA, DRE and combination of both indications were 53%, 58% and 67.3% respectively while the PPVs were 48.3%, 51.9% and 61.2% respectively. Mean Gleason score was 6.82 while the overall complication rate was 23.2%

CONCLUSION: Neither PSA nor DRE is sensitive, specific, predictive or accurate enough on its own to be an ideal screening or diagnostic test for CaP. Therefore, optimal evaluation of patients with suspected CaP is best achieved with both even in unscreened populations.

[1135] TÍTULO / TITLE: - Ability of Biochemical Parameters to Distinguish between Bile Duct Cancer and Gall Bladder Stones - A Case Control Study in a Tertiary Care Hospital of Pokhara Valley.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Yadav SK; Mittal A; Sapkota K; Gupta SP; Sathian B
INSTITUCIÓN / INSTITUTION: - Department of Biochemistry, Manipal College of Medical Sciences, Pokhara, Nepal E-mail: shambhuyadav47@gmail.com.
RESUMEN / SUMMARY: - Background: The present study was designed to comparatively assess alteration of biochemical parameters in bile duct cancer and gall stone disease. Materials and Methods: A hospital based case-control study was carried out in the Department of Biochemistry of Manipal Teaching Hospital, Pokhara, Nepal between 1st January 2010 and 31st December 2012. The variables collected were age, gender, serum total cholesterol, total bilirubin, AST, ALT, serum alkaline phosphatase, albumin and hemoglobin. One way ANOVA was used to examine the statistical significance of differences between groups. A post-hoc LSD test was applied for the comparison of means of control versus case groups. A p-value of <0.05 (two-tailed) was considered significant.
Results: The mean age of cases and controls was 53.2+/−21.2 years. The levels of serum cholesterol were higher in cases of cancer 192.5+/−21.5 mg/dl in comparison to stone cases 168.7+/−16.1 mg/dl (p value: 0.0001). The total bilirubin showed the marked difference in cases of cancer 7.6+/−3.2 mg/dl in comparison to stone cases 2.5+/−0.8 mg/dl of bile duct. There was discernible divergence in values of alkaline phosphatase in cases of cancer 251.5+/−20.1 IU/l when compared to stone cases 173.2+/−12.6 IU/l of bile duct. In contrast, there was no apparent deviation in values of aspartate transaminases and alanine transaminases in cases of cancer 59.1+/−8.9 IU/l and 105.5+/−26.5 IU/l when compared to stone cases 56.9+/−7.9 IU/l and 84.5+/−13.5 IU/l respectively.
Conclusions: LFT analysis for pre-operative assessment was a good predictive marker in setting apart bile duct cancer and gall bladder stone.

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TÍTULO/TITLE: - Association between Urinary Prostaglandin E2 Metabolite and Breast Cancer Risk: A Prospective, Case-Cohort Study of Postmenopausal Women.

RESUMEN/SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES/AUTHORS: - Kim S; Taylor JA; Milne GL; Sandler DP

INSTITUCIÓN/INSTITUTION: - Georgia Regents University Cancer Center, Medical College of Georgia, Section of Hematology/Oncology, Department of Medicine, 1410 Laney Walker Blvd., Augusta, GA 30912. sankim@gru.edu.

RESUMEN/SUMMARY: - Overweight or obese women are at increased risk of developing and dying from breast cancer. Obesity-driven inflammation may stimulate prostaglandin E2 (PGE2)-mediated aromatase activation and estrogen biosynthesis in breast tissues. We hypothesized that increased production of PGE2 would contribute to elevated breast cancer risk in postmenopausal women. We carried out a case-cohort study with 307 incident breast cancer cases and 300 subcohort members from the Sister Study cohort. HRs and 95% confidence intervals (CI) were estimated for the association between urinary levels of a major PGE2 metabolite (PGE-M) and breast cancer risk using Prentice’s pseudo-likelihood approach. Several lifestyle factors were associated with urinary levels of PGE-M: smoking, high-saturated fat diet, and obesity increased urinary PGE-M, and use of nonsteroidal antiinflammatory drugs (NSAID) decreased urinary PGE-M. Although there was no association between urinary PGE-M and postmenopausal breast cancer risk in the overall analysis or among regular users of NSAIDs, there was a positive association among postmenopausal women who did not regularly use NSAIDs with HRs of 2.1 [95% confidence interval (CI): 1.0-4.3]; 2.0 (95% CI: 1.0-3.9); and 2.2 (95% CI: 1.1-4.3) for the second, third, and highest quartiles of PGE-M. Our findings suggest a link between systemic PGE2 formation and postmenopausal breast cancer, and a possible modification of the association by lifestyle and pharmacologic interventions. If confirmed in larger studies, these results may have useful implications for the development of preventive strategies. Cancer Prev Res; 6(6); 511-8. ©2013 AACR.

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[1137]
**Título / Title:** - Evaluation of Absorbed Dose from Kilovoltage Cone-beam Computed Tomography by Radiotherapy Planning System: Influence on the Radiation Therapy for Prostate Cancer.

**Resumen / Summary:** - Enlace al Resumen / Link to its Summary


**Autores / Authors:** - Kawamura T; Murakami N; Okamura Y; Nishimura H; Miyawaki D; Kimura K; Hase M; Sasaki R

**Institución / Institution:** - Department of Radiology, Kakogawa West City Hospital.

**Resumen / Summary:** - Image-guided radiation therapy (IGRT) is increasingly being used in modern radiation therapy, and it is now possible to verify a patient's position using kilo-voltage cone-beam computed tomography (kV-CBCT). However, if kV-CBCT is used frequently, the dose absorbed by the body cannot be disregarded. A number of studies have been made on the absorbed dose of kV-CBCT, in which absorbed dose measurements were made using a computed tomography dose index (CTDI) or a thermoluminescent dosimeter (TLD). Other methods include comparison of the absorbed dose between a kV-CBCT and other modalities. These techniques are now in common use. However, dose distribution within the patient varies with the patient's size, posture and the part of the body to which radiation therapy is applied. The chief purpose of this study was to evaluate the dose distribution of kV-CBCT by employing a radiotherapy planning system (RTPS); a secondary aim was to examine the influence of a dose of kV-CBCT radiation when used to treat prostate cancer. The beam data of an on-board imager (OBI) was registered in the RTPS, after which modeling was performed. The radiation dosimetry was arranged by the dosimeter in an elliptical phantom. Rotational radiation treatment was used to obtain the dose distribution of the kV-CBCT within the patient, and the patient dose was evaluated based on the simulation of the dose distribution. In radiation therapy for prostate cancer, if kV-CBCT was applied daily, the dose increment within the planning target volume (PTV) and the organ in question was about 1 Gy.

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**Título / Title:** - Penile cancer: diagnosis, clinical features and management.

**Resumen / Summary:** - Enlace al Resumen / Link to its Summary

**Revista / Journal:** - Nurs Stand. 2013 Mar 20-26;27(29):50-7; quiz 58.

**Autores / Authors:** - Turner B; Drudge-Coates L; Henderson S

**Institución / Institution:** - Department of Urology, Homerton University Hospital, London. bruce.turner@homerton.nhs.uk

**Resumen / Summary:** - This article aims to provide the reader with an overview of penile cancer. The focus is on clinical and medical aspects to help nurses understand incidence, aetiology, diagnosis and treatment, to enable them
educate and support patients affected by this disease. Psychological support of patients and their partners is also emphasised as the effects of penile cancer can be significant.

[1139]
TÍTULO / TITLE: - Effect of IL-18 gene promoter polymorphisms on prostate cancer occurrence and prognosis in Han Chinese population.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Liu JM; Liu JN; Wei MT; He YZ; Zhou Y; Song XB; Ying BW; Huang J
INSTITUCIÓN / INSTITUTION: - Department of Urology Surgery, West China School of Medicine, West China Hospital, Sichuan University, Sichuan Province, P.R. China.
RESUMEN / SUMMARY: - Interleukin-18 (IL-18) has been implicated in a wide variety of cellular functions that affect the biological response to tumors. However, there is insufficient evidence to prove that IL-18 gene variants are associated with risk of prostate cancer. We examined a possible association between two promoter polymorphisms, -137G/C (rs187238) and -607C/A (rs1946518), in the IL-18 gene and prostate cancer occurrence and prognosis in Han Chinese. We used a high-resolution melting method to genotype these two polymorphisms in 375 Chinese Han patients with prostate cancer and in 400 age-matched healthy controls. A hundred and eighty-one prostate cancer patients who had been receiving androgen deprivation therapy, including operational and medical castration, were enrolled to follow-up in this study. Carriers of the GG genotype of the -137G/C polymorphism had a 2.165-times higher risk of prostate cancer progression than carriers of GC [95% confidence interval (CI) = 1.270-3.687]. Patients with the GG genotype at clinical stages III and IV also had significantly lower rates of progression-free survival (relative risk = 2.174, 95%CI = 1.211-3.906). However, we found no significant association of genotype or allele distributions of these two polymorphisms with occurrence of prostate cancer. We conclude that there is evidence that the IL-18 gene promoter polymorphism -137G/C influences the prognosis of prostate cancer patients in androgen deprivation therapy, although neither of the two SNPs contributes to prostate cancer development.

[1140]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Prostate cancer (PCa) is the most commonly diagnosed male malignancy and the second biggest cause of cancer death in men of the Western world. Higher incidences of PCa occur in men from North America, Oceania and Western countries, whereas men from Asia and North Africa have a much lower PCa incidence rate. Investigations into this population disparity of PCa incidence, in order to identify potential preventive factors or targets for the therapeutic intervention of PCa, have found differences in both environmental and genetic variations between these populations. Environmental variations include both diet and lifestyle, which vary widely between populations. Evidence that diet comes into play has been shown by men who immigrate from Eastern to Western countries. PCa incidence in these men is higher than men in their native countries. However the number of immigrants developing PCa still doesn’t match native black/white men, therefore genetic factors also contribute to PCa risk, which are supported by familial studies. There are a number of genetic polymorphisms that are differentially presented between Western and Eastern men, which are potentially associated with PCa incidence. Androgen and its receptor (AR) play a major role in PCa development and progression. In this study, we focus on genes involved in androgen biosynthesis and metabolism, as well as those associated with AR pathway, whose polymorphisms affect androgen level and biological or physiological functions of androgen. While many of the genetic polymorphisms in this androgen/AR system showed different frequencies between populations, contradictory evidences exist for most of these genes investigated individually as to the true contribution to PCa risk. More accurate measurements of androgen activity within the prostate are required and further studies need to include more African and Asian subjects. As many of these genetic polymorphisms may contribute to different steps in the same biological/physiological function of androgen and AR pathway, an integrated analysis considering the combined effect of all the genetic polymorphisms may be necessary to assess their contribution to PCa initiation and progression.
INTRODUCTION: Periprostatic nerve block (PPNB) is a common local anaesthetic technique in transrectal ultrasound-guided (TRUS) prostate biopsy, but concerns remain over the increased theoretical risks of urinary tract infection (UTI) and sepsis from the additional transrectal needle punctures. This study reviewed our biopsy data to assess this risk. Materials and Methods: Retrospective data collected from 177 men who underwent TRUS biopsy between July 2007 and December 2009 in a single institution were analysed. PPNB was administered using 1% xylocaine at the prostatic base and apex and repeated on the contralateral side under ultrasound guidance. Complications, including UTI sepsis, bleeding per rectum and acute retention of urine (ARU) were noted. Every patient was tracked for the first 2 weeks for complications until his clinic review. Demographic profile, biopsy parameters and histological findings were reviewed. Univariate and multivariate analysis of possible risk factors for development of sepsis after TRUS biopsy were performed. Statistical analysis was performed using SPSS 17.0. Results: Ninety (51%) men received PPNB and 87 (49%) did not. The groups were matched in age (PPNB: mean 62.7 +/- 5.8 years; without PPNB: mean 64.4 +/- 5.7 years) and prebiopsy prostate specific antigen (PSA) levels (PPNB: mean 8.2 +/- 3.9 ng/mL; without PPNB: mean 8.3 +/- 3.7 ng/mL). The PPNB group had a larger prostate volume, with more cores taken (P <0.05). On univariate and multivariate analysis controlling for age, PSA, prostate volume, number of cores taken and histological prostatitis, PPNB was not a significant risk factor for sepsis. Sepsis rates were 5.6% in the PPNB group and 5.7% in the other group (P = 0.956). Overall prostate cancer detection rate was 33.3%. Conclusion: The risk of sepsis was not increased in patients who received PPNB, even though this group had larger gland volumes and more biopsy cores taken.

[1142]
TITULO / TITLE: - Metronomic administration of chlorambucil for treatment of dogs with urinary bladder transitional cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Schrempp DR; Childress MO; Stewart JC; Leach TN; Tan KM; Abbo AH; de Gortari AE; Bonney PL; Knapp DW
INSTITUCION / INSTITUTION: - Department of Veterinary Clinical Sciences, Purdue University, West Lafayette, IN 47907.
Objective-To determine the antitumor effects and toxicoses of metronomic oral administration of a low dose of chlorambucil in dogs with transitional cell carcinoma (TCC). Design-Prospective clinical trial. Animals-31 client-owned dogs with TCC for which prior treatments had failed or owners had declined other treatments. Procedures-Chlorambucil (4 mg/m(2), PO, q 24 h) was administered to dogs. Before and at scheduled times during treatment, evaluations of dogs included physical examination, CBC, serum biochemical analyses, urinalysis, thoracic and abdominal imaging including cystosonography for measurement of TCCs, and grading of toxicoses. Results-29 of 31 dogs had failed prior TCC treatment. Of the 30 dogs with available data, 1 (3%) had partial remission (>= 50% reduction in tumor volume), 20 (67%) had stable disease (< 50% change in tumor volume), and 9 (30%) had progressive disease (>= 50% increase in tumor volume or development of additional tumors); 1 dog was lost to follow-up. The median progression-free interval (time from the start of chlorambucil treatment to the day progressive disease was detected) for the dogs was 119 days (range, 7 to 728 days). The median survival time of dogs from the time of the start of chlorambucil treatment was 221 days (range, 7 to 747 days). Few toxicoses were detected; chlorambucil administration was discontinued because of toxicoses in only 1 dog. Conclusions and Clinical Relevance-Metronomic administration of chlorambucil was well tolerated, and 70% of dogs had partial remission or stable disease. Metronomic administration of chlorambucil may be a treatment option for dogs with TCC.

Robotic mechanical localization of prostate cancer correlates with magnetic resonance imaging scans.

Purpose: To evaluate the concordance of cancer location of the tissue mapping from a mechanical pressure transducer with magnetic resonance imaging (MRI) scans. Materials and Methods: A total of 60 indentations were performed on 5 prostate specimens obtained after radical prostatectomy utilizing a robotic indentation system. The mechanical elastic moduli of suspected malignant lesions were calculated and mapped, and their locations were compared with suspicious areas of malignancy on MRI scans.
Results: The concordance rate between the location mapping from the robotic indentation system and MRI scans results was 90.0% (54/60). The sensitivity and specificity of the robotic indentation system were 87.9% (29/33) and 92.6% (25/27), respectively. The positive predictive value and negative predictive value were 93.5% (29/31) and 93.1% (27/29), respectively. Conclusion: The locations of malignant lesions derived from our robotic indentation system correlated strongly with the locations of suspected areas of malignancy on MRI scans. Our robotic system may provide a more targeted biopsy of the prostate than conventional non-targeted systemic biopsy, possibly improving the diagnostic accuracy of prostatic biopsies for cancer.

[1144]
TÍTULO / TITLE: Reduced mRNA expression level of corticotropin-releasing hormone-binding protein is associated with aggressive human kidney cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Tezval H; Atschekzei F; Peters I; Waalkes S; Hennenlotter J; Stenzl A; Becker JU; Merseburger AS; Kuczyk MA; Serth J
INSTITUCIÓN / INSTITUTION: Department of Urology and Urological Oncology, Hannover Medical School, Hannover, Germany. tezval.hossein@mh-hannover.de.
RESUMEN / SUMMARY: BACKGROUND: Significance of Urocortin (Ucn or Ucn1), Ucn2, Ucn3 and their receptors, Corticotropin Releasing Factor Receptor 1 and 2 (CRFR1 and CRFR2), and the binding protein, Corticotropin-Releasing Hormone-Binding Protein (CRHBP) in oncology is growing rapidly. The objective of our study was to assess the expression of the CRHBP mRNA and protein in renal cancer. METHODS: Tumoral tissues of 78 patients with clear cell renal cell cancer and their corresponding normal tissues were analyzed using quantitative mRNA expression analysis for detection of mRNA expression level. Protein expression and tissue localization of CRHBP protein in renal specimens was evaluated using western blotting, immunohistochemistry and double immunofluorescence, respectively. RESULTS: We found an approx. 33 fold decrease of average CRHBP mRNA level in tumoral tissues compared to paired normal tissues (p<0.001). Diminished CRHBP mRNA expression was positively correlated with advanced, metastasized and higher stage of disease (p<0.001, p=0.026, p=0.028 respectively). CRHBP protein was detected in glomeruli and proximal tubules of normal kidney while none or weak immunopositivity was found in cc-RCC (p<0.001). CONCLUSIONS: The expression analysis of CRHBP shows that cc-RCC is characterized by a significant loss of CRHBP mRNA expression that furthermore is associated
with a more aggressive state of tumors. Depletion of CRHBP proteins also indicate that the protein as part of the UCN system may be involved in renal carcinogenesis.

[1145]
TÍTULO / TITLE: - SPDEF: a molecular switch for E-cadherin expression that promotes prostate cancer metastasis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Osisami M; Keller ET

[1146]
TÍTULO / TITLE: - Productive infection of bovine papillomavirus type 2 in the urothelial cells of naturally occurring urinary bladder tumors in cattle and water buffaloes.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Roperto S; Russo V; Ozkul A; Corteggio A; Sepici-Dincel A; Catoi C; Esposito I; Riccardi MG; Urraro C; Luca R; Ceccarelli DM; Longo M; Roperto F
INSTITUCIÓN / INSTITUTION: - Dipartimento di Medicina Veterinaria e Produzioni Animali, Sezione Malattie Infettive, Universita di Napoli Federico II, Naples, Italy.
RESUMEN / SUMMARY: - BACKGROUND: Papillomaviruses (PVs) are highly epitheliotropic as they usually establish productive infections within squamous epithelia of the skin, the anogenital tract and the oral cavity. In this study, early (E) and late (L) protein expression of bovine papillomavirus type 2 (BPV-2) in the urothelium of the urinary bladder is described in cows and water buffaloes suffering from naturally occurring papillomavirus-associated urothelial bladder tumors. METHODS AND FINDINGS: E5 protein, the major oncoprotein of the BPV-2, was detected in all tumors. L1 DNA was amplified by PCR, cloned and sequenced and confirmed to be L1 DNA. The major capsid protein, L1, believed to be only expressed in productive papillomavirus infection was detected by Western blot analysis. Immunohistochemical investigations confirmed the presence of L1 protein both in the cytoplasm and nuclei of cells of the neoplastic urothelium. Finally, the early protein E2, required for viral DNA replication and known to be a pivotal factor for both productive and persistent infection, was detected by Western blot and immunohistochemically. Electron
microscopic investigations detected electron dense particles, the shape and size of which are consistent with submicroscopic features of viral particles, in nuclei of neoplastic urothelium. CONCLUSION: This study shows that both active and productive infections by BPV-2 in the urothelium of the bovine and bubaline urinary bladder can occur in vivo.

[1147]

TÍTULO / TITLE: - Genetic susceptibility loci, pesticide exposure and prostate cancer risk.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Koutros S; Berndt SI; Hughes Barry K; Andreotti G; Hoppin JA; Sandler DP; Yeager M; Burdett LA; Yuenger J; Alavanja MC; Beane Freeman LE

INSTITUCIÓN / INSTITUTION: - Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland, United States of America. KoutrosS@mail.nih.gov

RESUMEN / SUMMARY: - Uncovering SNP (single nucleotide polymorphisms)-environment interactions can generate new hypotheses about the function of poorly characterized genetic variants and environmental factors, like pesticides. We evaluated SNP-environment interactions between 30 confirmed prostate cancer susceptibility loci and 45 pesticides and prostate cancer risk in 776 cases and 1,444 controls in the Agricultural Health Study. We used unconditional logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Multiplicative SNP-pesticide interactions were calculated using a likelihood ratio test. After correction for multiple tests using the False Discovery Rate method, two interactions remained noteworthy. Among men carrying two T alleles at rs2710647 in EH domain binding protein 1 (EHBP1) SNP, the risk of prostate cancer in those with high malathion use was 3.43 times those with no use (95% CI: 1.44-8.15) (P-interaction= 0.003). Among men carrying two A alleles at rs7679673 in TET2, the risk of prostate cancer associated with high aldrin use was 3.67 times those with no use (95% CI: 1.43, 9.41) (P-interaction= 0.006). In contrast, associations were null for other genotypes. Although additional studies are needed and the exact mechanisms are unknown, this study suggests known genetic susceptibility loci may modify the risk between pesticide use and prostate cancer.

[1148]
TITULO / TITLE: - Application of (18)F-FDG PET/CT imaging in diagnosing bladder tumor metastasis lesions.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Li Y; Yang ZQ; Ye H; Qi L; Hu JW

INSTITUCIÓN / INSTITUTION: - Department of Urology, Xiangya Hospital, Central South University, Changsha, 410008, China, liyang7365@163.com.

RESUMEN / SUMMARY: - Bladder tumor is the most common malignant tumor in urinary system and always companied with lymph node metastasis. The accurate staging plays a significant role in treatment for bladder tumor and prognostic evaluation, and the distant metastasis predicts worse prognosis. The objective of this study was to assess the clinical significance of (18)F-FDG PET/CT imaging in diagnosing bladder tumor metastasis lesions. A retrospective analysis of 60 patients with bladder tumor from October 2008 to May 2010 was done. The patients were stratified based on the imaging technique. Among all 60 cases, besides the primary lesion, 81 suspected lesions were spotted and 73 confirmed as metastasis, including 50 lymph node metastases, 22 distant metastases, and 1 bone metastasis. For PET/CT imaging, its sensitivity was 94.5%, specificity 87.5%, positive predictive value 98.6%, negative predictive value 63.6% and accuracy 93.8% respectively. For CT, its sensitivity was 82.2%, specificity 50%, positive predictive value 93.8%, negative predictive value 23.5% and accuracy 79% respectively. PET/CT imaging was superior to CT in sensitivity, specificity and accuracy. In conclusion, (18)F-FDG PET/CT imaging is more significant in diagnosing bladder tumor metastasis lesions.

[1149]

TITULO / TITLE: - The ubiquitin ligase Siah2 is revealed as an accomplice of the androgen receptor in castration resistant prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Freeman MR

[1150]

TITULO / TITLE: - Differences in the expression of telomerase and prostate-specific membrane antigen in non-advanced prostatic cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
RESUMEN / SUMMARY: - Early recognition of prostate cancer (PC) based on biological markers could be helpful in identification of differences in benign and malignant lesions and facilitate further precise indication for more aggressive treatment. Therefore, the aim of our study was to assess expression of hTERT (human telomerase reverse transcriptase, a catalytic subunit of telomerase) and prostate-specific membrane antigen (PSMA), both considered to be markers of tumor aggressiveness. 140 low advanced PC specimens from patients who underwent radical prostatectomy were studied. Protein expression was assessed immunohistochemically on tumor sections and expressed as labeling index (LI), i.e. the percentage of positively stained cells. In case of telomerase, only nuclear staining and in case of PSMA, membrane and cytoplasmic staining, were considered as positive. The mean age of the patients was 62.9 +/- 6.2 years. There were 75 (53.6%) well differentiated tumors (Gleason score <\= 6), 52 (37.1%) moderately differentiated tumors (Gleason score of 7) and 13 (9.3%) poorly differentiated tumors (Gleason score 8-10). The mean pre-operative serum PSA was 9.9 +/- 5.5 ng/mL, and the mean LI were 18.0 +/- 1.5% and 44.1 +/- 1.9%, for hTERT and PSMA, respectively. With increase of pathological tumor stage and tumor grade statistically significant increase of PSA serum concentration (P < 0.011) and PSMA (P < 0.004) expression was noticed, however, for expression of telomerase the relation was opposite one. The observed in higher pTNM stages and tumor grades decrease in nuclear expression of hTERT was caused by translocation of the subunit to the cytoplasm, what may indicate extranuclear telomerase activity independent of telomere lengthening, hence, it cannot be considered as a marker of malignancy. Higher PSMA expression in higher pTNM stages and tumor grades suggest that PSMA may be a good marker of biological aggressiveness suitable for patients' selection for more aggressive treatment. (Folia Histochemica et Cytobiologica 2013, Vol. 51, No. 1, 66-72).
In renal cell carcinoma (RCC), single members of the Wnt/beta-catenin signaling cascade were recently identified to contribute to cancer progression. However, the role of Wnt1, one of the key ligands in beta-catenin regulation, is currently unknown in RCC. Therefore, alterations of the Wnt1/beta-catenin axis in clear cell RCC (ccRCC) were examined with regard to clinicopathology, overall survival (OS) and cancer specific survival (CSS). Corresponding ccRCCs and benign renal tissue were analyzed in 278 patients for Wnt1 and beta-catenin expression by immunohistochemistry in tissue microarrays. Expression scores, including intensity and percentage of stained cells, were compared between normal kidney and ccRCCs. Data was categorized according to mean expression scores and correlated to tumor and patients’ characteristics. Survival was analyzed according to the Kaplan-Meier and log-rank test. Univariable and multivariable Cox proportional hazard regression models were used to explore the independent prognostic value of Wnt1 and beta-catenin. In ccRCCs, high Wnt1 was associated with increased tumor diameter, stage and vascular invasion (p <= 0.02). High membranous beta-catenin was associated with advanced stage, vascular invasion and tumor necrosis (p <= 0.01). Higher diameter, stage, node involvement, grade, vascular invasion and sarcomatoid differentiation (p <= 0.01) were found in patients with high cytoplasmic beta-catenin. Patients with a high cytoplasmic beta-catenin had a significantly reduced OS (hazard ratio (HR) 1.75) and CSS (HR 2.26), which was not independently associated with OS and CSS after adjustment in the multivariable model. Increased ccRCC aggressiveness was reflected by an altered Wnt1/beta-catenin signaling. Cytoplasmic beta-catenin was identified as the most promising candidate associated with unfavorable clinicopathology and impaired survival. Nevertheless, the shift of membranous beta-catenin to the cytoplasm with a subsequently increased nuclear expression, as shown for other malignancies, could not be demonstrated to be present in ccRCC.

[1152]
TÍTULO / TITLE: Daily life and life quality 3 years following prostate cancer treatment.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

Enlace al texto completo (gratuito o de pago) 3390/ijms140610944
AUTORES / AUTHORS: Kruck S; Eyrich C; Scharpf M; Sievert KD; Fend F; Stenzl A; Bedke J
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Enlace al texto completo (gratuito o de pago) 1186/1472-6955-12-11
RESUMEN / SUMMARY: - BACKGROUND: Knowledge of experiences from prostate cancer is sparse in a longitudinal perspective. From a nursing perspective, results from combined qualitative and quantitative studies are lacking however would present the broadest knowledge base for best practice. Present descriptions of medical-physical symptoms such as urinary, bowel and sexual dysfunction from quantitative inquiries need be complemented with qualitative results. Such knowledge is essential in relation to treatment and communication with patients over the years and not only shortly after surgery.

METHODS: A longitudinal study was formatted to investigate general and specific health quality and sense of coherence quantitative alterations over three years. A general health quality module (EORTC QLC-C30) and a disease-specific module (EORTC PR-25) were applied for the longitudinal study together with the Orientation to life questionnaire (SOC), measuring a persons’ sense of coherence. In order to strengthen reliability and compensate for low participation we used the Directed content analysis for interviewing and analysis. The method allows using findings from earlier research when interviewing along with detecting new areas. Twenty-one men were followed over three years and six of them, in the third year, accepted to be interviewed.

RESULTS: We found high quality of life ratings and extended the study with follow-up interviews in year three, to investigate whether questionnaire results were in line with interview findings. We found high life quality and functioning ratings that were in line with qualitative descriptions. Interview analysis showed retrieval of life as lived before, yet in a different way, the men never forgot the diagnosis event, had a unique illness history worth hearing, and had come to terms with most treatment-related shortcomings. Sense of coherence ratings were medium to high and confirmed stability over time in comprehensibility, manageability and meaningfulness after prostate cancer treatment.

CONCLUSIONS: Over the years, the men’s negative experiences from shifted into ‘a good life’ though in a different way than before. The interpretation is supported in the study by quantitative results showing a high degree of functioning. The men’s sense of coherence seamed to support their handling of life three years after prostate cancer treatment.

[1153] TÍTULO / TITLE: - Valproic acid upregulates NKG2D ligand expression and enhances susceptibility of human renal carcinoma cells to NK cell-mediated cytotoxicity.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

ENLACE AL TEXTO COMPLETO (GRATUITO O DE PAGO): 5114/aoms.2013.34413

AUTORES / AUTHORS: Yang F; Shao Y; Yang F; Liu M; Huang J; Zhu K; Guo C; Luo J; Li W; Yang B; Shi J; Zheng J

INSTITUCIÓN / INSTITUTION: Department of Urology, Tenth People’s Hospital of Tongji University, Shanghai, China.

RESUMEN / SUMMARY: INTRODUCTION: We aimed to investigate the effect of valproic acid (VPA) on NKG2D ligand expression in human renal carcinoma cell lines and to investigate the mechanisms. MATERIAL AND METHODS: Different concentrations of VPA from 0.5 mM to 8.0 mM were applied to 786-O and ACHN cell lines, respectively. Cell viability after treatment with VPA was determined by flow cytometry (FCM). Real-time PCR and FCM were used to detect the changes of mRNA and protein level of NKG2D ligands (MICA/B and ULBPs) in the two cell lines treated with 4 mM VPA. The cytotoxicity assay and CD107a mobilization assay were carried out to detect the cytotoxicity changes of NK cells against renal carcinoma cell lines after the same treatment. RESULTS: Valproic acid can efficiently upregulate MICA/B, ULBP1 and ULBP2 expression in the renal carcinoma cell lines at the mRNA and protein level (p < 0.05). 786-O and ACHN cells treated with VPA were more susceptible to killing by NK cells than untreated cells and the enhanced cytotoxicity of NK cells was blocked by the pretreatment of NK cells with anti-NKG2D monoclonal antibodies (p < 0.05). CONCLUSIONS: Valproic acid can clearly induce the expression of NKG2D ligands of renal carcinoma cell lines, thereby enhancing the cytotoxicity of NK cells against renal carcinoma cell lines.

TÍTULO / TITLE: Effects of oleic acid on cell proliferation through an integrin-linked kinase signaling pathway in 786-O renal cell carcinoma cells.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


ENLACE AL TEXTO COMPLETO (GRATUITO O DE PAGO): 3892/ol.2013.1160

AUTORES / AUTHORS: Liu Z; Xiao Y; Yuan Y; Zhang X; Qin C; Xie J; Hao Y; Xu T; Wang X

INSTITUCIÓN / INSTITUTION: Department of Urology, Peking University People’s Hospital, Beijing 100044, P.R. China.

RESUMEN / SUMMARY: An increased risk of renal cell carcinoma (RCC) has been linked with obesity and metabolic syndrome. However, the mechanisms by which lipid metabolic disorders affect the development of RCC remain unclear and highly controversial. Integrin-linked kinase (ILK) is a serine/threonine protein kinase involved in the regulation of tumor cell growth and angiogenesis. In the present study, the effect of free fatty acids in the promotion of RCC progression was investigated by upregulating ILK. Results of
the MTT assay indicated that treatment of 786-O cells with oleic acid induced a concentration-dependent increase in cell viability. Flow cytometry analysis revealed that the effect of oleic acid on cell apoptosis was not significant. Following treatment with oleic acid, the expression of ILK, phospho-Akt and G protein-coupled receptor 40 (GPR40) was increased in 786-O cells. These effects were reversed when the expression of ILK was downregulated using specific small interfering RNA. These results indicate that free fatty acids are associated with the development of renal cell carcinoma via activation of the GPR40/ILK/Akt pathway, revealing a novel mechanism for the correlation between metabolic disturbance and renal carcinoma.

[1155]

TÍTULO / TITLE: - The potential role of anti tumor necrosis factor-alpha antibodies on some renal functions and vasoregulatory factors in preeclamptic pregnant Wistar rats.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Gad HI

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RESUMEN / SUMMARY: - OBJECTIVE: To investigate the potential role of anti-tumor necrosis factor-alpha (TNF-alpha) antibodies on some renal functions and release of vasoregulatory peptides using nitric oxide synthase deprived pregnant rats. METHODS: This study was carried out at King Khalid University Hospital, King Saud University, Riyadh, Kingdom of Saudi Arabia from December 2011 to November 2012. Forty female Wistar rats were divided into 4 groups (10 rats each); Group I - included virgin non-pregnant rats. Group II - included pregnant rats that received saline, Group III - received NG-nitro-L-arginine methyl ester (L-NAME), and Group IV - received both L-NAME and anti TNF-alpha antibodies. Mean arterial blood pressure, urine volume, creatinine clearance and 24 hours urinary albumin excretion were measured on day 20 of gestation. Blood samples were taken on day 20 of gestation for measurement of plasma endothelin-1 (ET-1), angiotensin II (Ag II) and serum levels of total nitric oxide (NO) products, interleukin-6 (IL-6) and soluble vascular cell adhesion molecule (sVCAM-1). Viable pups were also weighed. RESULTS: Anti TNF-alpha antibodies reversed hypertension, improved renal function, decreased release of vasoactive substances and increased pup weight. CONCLUSION: Preeclampsia is associated with disturbed renal function, overproduction of cytokines and vasoregulatory factors, and fetal growth restriction. Treatment of pregnant rats with anti TNF-alpha antibodies, restored urine volume, creatinine clearance, plasma ET-1, serum IL-6 and sVCAM-1 to normal levels. Hence, anti
TNF-alpha antibodies may have beneficial effects in preeclampsia. Additional studies are warranted to confirm these results.
Most cholecystocutaneous fistulas are postoperative complications of liver and biliary tract surgery or trauma. External biliary fistulas rarely occur spontaneously as a result of intrahepatic abscess (pyogenic or parasitic), necrosis or perforation of the gallbladder, or other inflammatory process involving the biliary tree. A cholecystocutaneous fistula as a presentation of an underlying cancer arising from the gall bladder is an extremely uncommon finding. Over the past 50 years fewer than 20 cases of spontaneous cholecystocutaneous fistulas have been described in the medical literature but so far there has been no published report of a cholecystocutaneous fistula arising from adenocarcinoma of gall bladder. We here report a case of a patient presenting with spontaneous cholecystocutaneous fistula from cancer of gall bladder.

[1158]

TÍTULO / TITLE: Decreased expression of RNA-binding motif protein 3 correlates with tumour progression and poor prognosis in urothelial bladder cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Boman K; Segersten U; Ahlgren G; Eberhard J; Uhlen M; Jirstrom K; Malmstrom PU

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RESUMEN / SUMMARY: BACKGROUND: Low nuclear expression of the RNA-binding motif protein 3 (RBM3) has previously been found to be associated with poor prognosis in several cancer forms e.g. breast, ovarian, colorectal, prostate cancer and malignant melanoma. The aim of this study was to examine the prognostic impact of RBM3 expression in urinary bladder cancer. METHODS: Immunohistochemical RBM3 expression was examined in tumours from 343 patients with urothelial bladder cancer. Chi-square and Spearman's correlation tests were applied to explore associations between RBM3 expression and clinicopathological characteristics. The impact of RBM3 expression on disease-
specific survival (DSS), 5-year overall survival (OS) and progression-free survival (PFS) was assessed by Kaplan-Meier analysis and Cox proportional hazards modelling. RESULTS: Reduced nuclear RBM3 expression was significantly associated with more advanced tumour (T) stage (p <0.001) and high grade tumours (p=0.004). Negative RBM3 expression was associated with a significantly shorter DSS (HR=2.55; 95% CI 1.68-3.86)) and 5-year OS (HR=2.10; 95% CI 1.56-2.82), also in multivariable analysis (HR=1.65; 95% CI 1.07-2.53 for DSS and HR=1.54; 95% CI 1.13-2.10 for 5-year OS). In patients with Ta and T1 tumours expressing reduced RBM3 levels, Kaplan-Meier analysis revealed a significantly shorter PFS (p=0.048) and 5-year OS (p=0.006). CONCLUSION: Loss of RBM3 expression is associated with clinically more aggressive tumours and an independent factor of poor prognosis in patients with urothelial bladder cancer and a potentially useful biomarker for treatment stratification and surveillance of disease progression.

[1159]
TÍTULO / TITLE: - MiR199b Suppresses Expression of Hypoxia-Inducible Factor 1alpha (HIF-1alpha) in Prostate Cancer Cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Shang W; Chen X; Nie L; Xu M; Chen N; Zeng H; Zhou Q

INSTITUCIÓN / INSTITUTION: - Laboratory of Pathology, State Key Laboratory of Biotherapy and Department of Pathology, West China Hospital, West China Medical School, Sichuan University, Chengdu 610041, China.

RESUMEN / SUMMARY: - MicroRNAs (miRNAs) are a class of small noncoding RNAs that post-transcriptionally repress expression of target genes via imperfect base-pairing with the 3′-untranslated region (3′-UTR). The transcription factor hypoxia-inducible factor-1alpha (HIF-1alpha) plays important roles in physiology and pathology. Constitutive over-expression of HIF-1alpha is observed in many types of cancers including prostate carcinoma, but the mechanisms underlying this event remain largely unknown. Here we investigated the expression of miR199b and HIF-1alpha in normal prostate tissue, prostate cancer tissues and prostate carcinoma (PCa) cell lines LNCaP, PC-3 and DU145. We found that miR-199b expression level was decreased in prostate cancer while HIF-1alpha was significantly over-expressed. Furthermore, we postulated the posttranscriptional regulation of HIF-1alpha by miR199b through bioinformatics analysis, and herein we experimentally demonstrated that miR199b negatively regulated HIF-1alpha by targeting its 3′-untranslated region. Artificial over-expression of miR199b by using adenoviral
vectors in prostate cancer PC-3 and DU145 cells significantly down-regulated HIF-1alpha, together with reduced cell growth and increased cell death.

[1160]

TÍTULO / TITLE: Variable metastatic potentials correlate with differential plectin and vimentin expression in syngeneic androgen independent prostate cancer cells.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Burch TC; Watson MT; Nyalwidhe JO

INSTITUCIÓN / INSTITUTION: Department of Microbiology and Molecular Cell Biology, Eastern Virginia Medical School, Norfolk, Virginia, United States of America; Leroy T. Canoles Jr. Cancer Research Center, Eastern Virginia Medical School, Norfolk, Virginia, United States of America.

RESUMEN / SUMMARY: Prostate cancer is a clinically heterogeneous disease, ranging from indolent asymptomatic disease to very aggressive metastatic and life threatening forms of the disease. Distant metastasis represents the major lethal cause of prostate cancer. The most critical clinical challenge in the management of the patients is identifying those individuals at risk of developing metastatic disease. To understand the molecular mechanisms of prostate cancer metastasis and identify markers with metastatic potential, we have analyzed protein expression in two syngeneic prostate cancer cells lines PC3-N2 and PC3-ML2 using isobaric tags for relative and absolute quantitation labeling and multi-dimensional protein identification technology liquid chromatography matrix assisted laser desorption ionization tandem mass spectrometry. PC3-N2 is lowly metastatic while PC3-ML2 highly metastatic. A total of 1,756 proteins were identified in the analyses with 130 proteins showing different expression levels (p<0.01) in the two cell lines. Out of these, 68 proteins were found to be significantly up-regulated while 62 are significantly down-regulated in PC3-ML2 cells compared with PC3-N2 cells. The upregulation of plectin and vimentin which were the most significantly differentially expressed were validated by Western blot and their functional relevance with respect to invasion and migration was determined by siRNA gene silencing. To our knowledge, this study is the first to demonstrate that up-regulation of vimentin and plectin expression positively correlates with the invasion and metastasis of androgen-independent PCA.

[1161]
TÍTULO / TITLE: - Missense allele of a single nucleotide polymorphism rs2294008 attenuated antitumor effects of prostate stem cell antigen in gallbladder cancer cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ono H; Chihara D; Chiwaki F; Yanagihara K; Sasaki H; Sakamoto H; Tanaka H; Yoshida T; Saeki N; Matsuo K

INSTITUCIÓN / INSTITUTION: - Division of Genetics, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Prostate stem cell antigen (PSCA), an organ-dependent tumor suppressor, is down regulated in gallbladder cancer (GBC). It is anticipated that the missense allele C of the single nucleotide polymorphism (SNP) rs2294008 (T/C) in the translation initiation codon of the gene affects the gene’s biological function and has some influence on GBC susceptibility. We examined the biological effect of the C allele on the function of the gene and the relation between the C allele and GBC susceptibility.

MATERIALS AND METHODS: Functional analysis of the SNP was conducted by introducing PSCA cDNA harboring the allele to a GBC cell line TGBC-1TKB and performing colony formation assays in vitro and tumor formation assays in mice. The effect on transcriptional regulation was assessed by reporter assays. The association study was conducted on 44 Japanese GBC cases and 173 controls. RESULTS: The PSCA cDNA harboring the C allele showed lower cell growth inhibition activity (20% reduction) than that with the T allele. Concordantly, when injected into subcutaneous tissues of mice, the GBC cell line stably expressing the cDNA with the C allele formed tumors of almost the same size as that of the control cells, but the cell line expressing the cDNA with the T allele showed slower growth. The upstream DNA fragment harboring the C allele had more transcriptional activity than that with the T allele. The C allele showed positive correlation to GBC but no statistical significant odds ratio (OR = 1.77, 95% confidence interval 0.85-3.70, P value = 0.127 in dominant model).

CONCLUSIONS: The missense allele was shown to have a biological effect, attenuating antitumor activities of PSCA, and consequently it may be a potential risk for GBC development. An association study in a larger sample size may reveal a significant association between the allele and GBC.

[1162] TÍTULO / TITLE: - Identification of nine genomic regions of amplification in urothelial carcinoma, correlation with stage, and potential prognostic and therapeutic value.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0060927

Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Chekaluk Y; Wu CL; Rosenberg J; Riester M; Dai Q; Lin S; Guo Y; McDougal WS; Kwiatkowski DJ

INSTITUCIÓN / INSTITUTION: - Division of Translational Medicine, Brigham and Women's Hospital, Boston, Massachusetts, United States of America.

RESUMEN / SUMMARY: - We performed a genome wide analysis of 164 urothelial carcinoma samples and 27 bladder cancer cell lines to identify copy number changes associated with disease characteristics, and examined the association of amplification events with stage and grade of disease. Multiplex inversion probe (MIP) analysis, a recently developed genomic technique, was used to study 80 urothelial carcinomas to identify mutations and copy number changes. Selected amplification events were then analyzed in a validation cohort of 84 bladder cancers by multiplex ligation-dependent probe assay (MLPA). In the MIP analysis, 44 regions of significant copy number change were identified using GISTIC. Nine gene-containing regions of amplification were selected for validation in the second cohort by MLPA. Amplification events at these 9 genomic regions were found to correlate strongly with stage, being seen in only 2 of 23 (9%) Ta grade 1 or 1-2 cancers, in contrast to 31 of 61 (51%) Ta grade 3 and T2 grade 2 cancers, p<0.001. These observations suggest that analysis of genomic amplification of these 9 regions might help distinguish non-invasive from invasive urothelial carcinoma, although further study is required. Both MIP and MLPA methods perform well on formalin-fixed paraffin-embedded DNA, enhancing their potential clinical use. Furthermore several of the amplified genes identified here (ERBB2, MDM2, CCND1) are potential therapeutic targets.

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[1163]

TÍTULO / TITLE: - HNF1b is involved in prostate cancer risk via modulating androgenic hormone effects and coordination with other genes.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hu YL; Zhong D; Pang F; Ning QY; Zhang YY; Li G; Wu JZ; Mo ZN

INSTITUCIÓN / INSTITUTION: - Medical Scientific Research Centre, Guangxi Medical University, Nanning, Guangxi Zhuang Autonomous Region, China.

RESUMEN / SUMMARY: - Prostate cancer is one of the most commonly diagnosed male malignancies. Genome wide association studies have revealed HNF1b to be a major risk gene for prostate cancer susceptibility. We examined
the mechanisms of involvement of HNF1b in prostate cancer development. We integrated data from Gene Expression Omnibus prostate cancer genes from the Dragon Database of Genes Implicated in Prostate Cancer, and used meta-analysis data to generate a panel of HNF1b-associated prostate cancer risk genes. An RT-PCR was used to assess expression levels in DU145, PC3, LNCaP, and RWEP-1 cells. Twelve genes (BAG1, DDR1, ERBB4, ESR1, HSPD1, IGFBP2, IGFBP5, NR4A1, PAWR, PIK3CG, RAP2A, and TPD52) were found to be associated with both HNF1b and prostate cancer risk. Six of them (BAG1, ERBB4, ESR1, HSPD1, NR4A1, and PIK3CG) were mapped to the KEGG pathway, and submitted to further gene expression assessment. HNF1b, NR4A1, and HSPD1 were found to be highly expressed in the LNCaP androgenic hormone-dependent cell line. Compared to expression levels in wild-type prostate cancer cells, NR4A1, HSPD1, ERBB4, and ESR1 expression levels were also found to be significantly increased in the HNF1b-transfected cells. We conclude that the mechanism of action of HNF1b in prostate cancer involves modulation of the association between androgenic hormone and prostate cancer cells. Gene-gene interaction and coordination should be taken into account to determine relationships between specific loci and diseases.

[1164]

**TÍTULO / TITLE:** XRCC1 Arg194Trp and Arg280His Polymorphisms Increase Bladder Cancer Risk in Asian Population: Evidence from a Meta-Analysis.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 10.1371/journal.pone.0064001

**AUTORES / AUTHORS:** Fang Z; Chen F; Wang X; Yi S; Chen W; Ye G

**INSTITUCIÓN / INSTITUTION:** Department of Urology, Center of Nephrology, The Second Affiliated Hospital of the Third Military Medical University, Chongqing, China.

**RESUMEN / SUMMARY:** BACKGROUND: A lot of studies have investigated the correlation between x-ray cross complementing group 1 (XRCC1) polymorphisms and bladder cancer risk, but the results in Asian population were still inconclusive. We conducted a meta-analysis to ascertain the association of XRCC1 Arg194Trp, Arg280His and Arg399Gln polymorphisms with bladder cancer risk in Asian population. METHODOLOGY/PRINCIPAL FINDINGS: The association strength was measured with odds ratios (ORs) and 95% confidence intervals (95% CIs). A total of 9 eligible studies, conducted in China, India and Japan, were identified. We observed a significant increased risk of bladder cancer in dominant model (OR = 1.199, 95% CI: 1.021,1.408, P heterogeneity = 0.372), allele comparison (OR = 1.200, 95% CI: 1.057,1.362, P heterogeneity = 0.107) of Arg194Trp, heterozygote comparison (OR = 1.869, 95% CI: 850
1.205, 2.898, Pheterogeneity = 0.011) and dominant model (OR = 1.748, 95% CI: 1.054, 2.900, Pheterogeneity = 0.01) of Arg280His. Pooled results estimated from adjusted ORs further validated these findings. No publication bias was detected. Subgroup analyses found that significant increased risk was only found among community-based studies not hospital-based studies. There was no evidence of publication bias. CONCLUSION: This is the first meta-analysis conducted in Asian investigating the correlation between XRCC1 polymorphisms and susceptibility to bladder cancer. Our meta-analysis shows that XRCC1 Arg194Trp and Arg280His polymorphisms are associated with a significantly increased risk of bladder cancer in Asian population.

[1165]

TÍTULO / TITLE: - The role of urinary fractionated metanephrines in the diagnosis of phaeochromocytoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Jeyaraman K; Natarajan V; Thomas N; Jacob PM; Nair A; Shanthly N; Oommen R; Varghese G; Joseph FJ; Seshadri MS; Rajaratnam S
INSTITUCIÓN / INSTITUTION: - Department of Endocrinology, Christian Medical College, Vellore, India.
RESUMEN / SUMMARY: - BACKGROUND & OBJECTIVES: Plasma and urinary metanephrines are used as screening tests for the diagnosis of phaeochromocytoma. The recommended cut-off levels are not standardized. This study was conducted to identify a cut-off level for 24 h urinary fractionated metanephrines viz. metanephrine (uMN) and normetanephrine (uNMN) using enzyme immunoassay for the diagnosis of phaeochromocytoma. METHODS: Consecutive patients suspected to have phaeochromocytoma were included in the study. uMN and uNMN in 24 h urinary sample were measured using a commercial ELISA kit. RESULTS: Overall, 72 patients were included over a period of 18 months. Twenty patients had histopathologically confirmed phaeochromocytoma and in 52 patients phaeochromocytoma was ruled out. Using the upper limit of normal stated by the assay manufacturer as the cut-off, uMN >350 mug/day had a low sensitivity and uNMN >600 mug/day had a poor specificity. By increasing the cut-off value of uNMN to twice the upper limit, specificity increased significantly without much loss in sensitivity. Combining uMN and uNMN using a cut-off twice the upper limit improved the diagnostic performance - sensitivity (95%); specificity (92.3%); positive predictive value (PPV - 82.6%); negative predictive value (NPV - 98%). In subsets of patients with a variable pretest probability for phaeochromocytoma, the PPV correlates well with the occurred of these tumors decreased, while the NPV remained at 100 per cent. INTERPRETATION & CONCLUSIONS: ELISA is a simple and reliable method for measuring uMN and uNMN. The test has a good NPV and
can be used as an initial screening test for ruling out phaeochromocytoma. Each hospital will have to define the cut-off value for the assay being used, choosing a proper control population.

[1166]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Thaidumrong T; Akarasakul D
INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Surgery, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok, Thailand. tncclinic@gmail.com
RESUMEN / SUMMARY: - BACKGROUND AND OBJECTIVE: At Rajavithi Hospital, open retropubic simple prostatectomy was started in 1985. The purpose of the present was to describe a surgical technique and early post-operative results of the first successful laparoscopic retropubic simple prostatectomy (LRSP) in Thailand. CASE REPORT: A 69-year-old Thai male presented with a chief complaint of refractory urinary retention. Digital rectal examination was performed with prostate gland of 4 finger breadths, firm consistency and smooth surface. The PSA level was 27.16 ng/ml. Transrectal ultrasound volume was 143 gm. The biopsy sample confirmed BPH and chronic prostatitis. The cystoscopy revealed prostate gland enlargement with obstruction. This patient’s manifestation required surgical treatment of BPH, and the LRSP technique was chosen. The prostatic capsule was incised by monopolar scissors and the prostatic adenoma was enucleated. The prostatic capsule was closed and a 22 Fr three-way irrigating Foley catheter was inserted. The operative time was 2 hours, with estimated blood loss of 600 ml and no immediate post-operative complications. The prostate specimen weighed 169 gm. The pathologic results confirmed BPH and prostatitis. Postoperative ambulation and catheter removal was on the 2nd and the 7th day, respectively. Postoperative uroflowmetry report showed a Qmax of 15 ml/s. CONCLUSION: Operated by an experienced laparoscopic team, laparoscopic retropubic simple prostatectomy for large BPH is a feasible alternative approach to open surgery.

[1167]
TÍTULO / TITLE: - A rare case of metastatic squamous urachal carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Squamous cell carcinoma is a very rare type of urachal malignancy, only a few cases being reported in the medical literature. We present the case of a 49-year-old male patient diagnosed with infected squamous cell urachal carcinoma with multiple pulmonary metastases, after complaints of lower abdominal pain, abdominal mass and fever, without respiratory symptoms. The abdominal ultrasonography and the CT scan revealed a tumoral mass in the lower abdomen in contact with the abdominal wall and the urinary bladder dome, displacing the small bowel. Pulmonary nodular lesions were described in the left lobe pyramid. The intraoperative diagnosis was necrotic urachal tumor with urinary bladder dome invasion and suspected pulmonary metastases, and tumor ablation with bladder dome resection and suture of the bladder were performed. The histopathological result was poorly differentiated squamous cell carcinoma (G3), with negative resection margins. The patient recovered well after surgery, but the prognosis is very poor due to the metastatic stage in which the tumor was diagnosed, no standard chemotherapy regimen for the treatment of metastatic urachal carcinoma being known as effective until now.
study. Demographic and medical data including age, performance status, tumor characteristics and comorbid diseases were collected from medical charts. Renal function was evaluated at least 48 hours before the treatment and at the end of the treatment based on the Modification of Diet in Renal Disease (MDRD) formula. Before and after cisplatin infusion serum NGAL levels were measured for the first and 3rd cycles of chemotherapy. Results: The median age of the study population was 54 (32-70) years. Fifteen patients (41.1%) were treated on an adjuvant basis, whereas 19 patients (58.9%) were treated for metastatic disease. There was no correlation of serum NGAL levels with serum creatinine ($r=0.20$, $p=0.26$) and MDRD ($r=-0.12$, $p=0.50$) and creatinine clearance-Cockcroft-Gault ($r=-0.22$, $p=0.22$) after cisplatin infusion at the end of the 3rd cycle of chemotherapy. Conclusions: In our study, serum NGAL levels were not correlated with the cisplatin induced nephrotoxicity. Further prospective studies are needed to conclude that serum NGAL level is not a good surrogate marker to predict early cisplatin induced nephrotoxicity.
is an independent predictor of PCa in men with PSA measuring 10-50 ng ml(-1). In clinical practice, particularly for those countries with lower incidences of PCa, PV should be considered when counselling patients with PSAs measuring 10-50 ng ml(-1) regarding their PCa risks.

[1170]
**TITULO / TITLE:** - Emergence of ETS transcription factors as diagnostic tools and therapeutic targets in prostate cancer.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** - Rahim S; Uren A
**INSTITUCIÓN / INSTITUTION:** - Lombardi Comprehensive Cancer Center, Georgetown University Washington DC.
**RESUMEN / SUMMARY:** - The discovery of chromosomal translocations in prostate cancer has greatly enhanced our understanding of prostate cancer biology. Genomic rearrangements involving the ETS family of transcription factors are estimated to be present in 50-70% of prostate cancer cases. These rearrangements fuse the ETS factors with promoters of genes that are androgen regulated. Thus, the expression of ETS factors, such as ERG, ETV1, ETV4 and ETV5, is mediated by androgen. In-vitro and in-vivo studies suggest that overexpression of ETS proteins increase cell proliferation and confer an invasive phenotype to prostate cancer cells. Epidemiological studies demonstrate that ETS-fusion positive patients exhibit tumors corresponding to a more advanced disease. The ability of ETS factors to serve as markers for screening and diagnosing prostate cancer patients is being investigated, and the results have been largely positive to date. Additionally, ETS factors present an excellent opportunity as therapeutic targets and several strategies have been devised to directly target ETS proteins or their binding partners and downstream effectors.

[1171]
**TITULO / TITLE:** - PMS1077 sensitizes TNF-alpha induced apoptosis in human prostate cancer cells by blocking NF-kappaB signaling pathway.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** - Shi J; Chen J; Serradji N; Xu X; Zhou H; Ma Y; Sun Z; Jiang P; Du Y; Yang J; Dong C; Wang Q
**INSTITUCIÓN / INSTITUTION:** - School of Life Sciences, Lanzhou University, Lanzhou, China.
RESUMEN / SUMMARY: - Our previous studies have demonstrated that PMS1077, a platelet-activating factor (PAF) antagonist, could induce apoptosis of Raji cells. However, the mechanism of action has not yet been determined. The nuclear transcription factor-kappa B (NF-kappaB) signaling pathway plays a critical role in tumor cell survival, proliferation, invasion, metastasis, and angiogenesis, so we determined the effects of PMS1077 and its structural analogs on tumor necrosis factor-alpha (TNF-alpha) induced activation of NF-kappaB signaling. In this study, we found that PMS1077 inhibited TNF-alpha induced expression of the NF-kappaB regulated reporter gene in a dose dependent manner. Western blot assay indicated that PMS1077 suppressed the TNF-alpha induced inhibitor of kappaB-alpha (IkappaB-alpha) phosphorylation, IkappaB-alpha degradation, and p65 phosphorylation. PMS1077 consistently blocked TNF-alpha induced p65 nuclear translocation as demonstrated in the immunofluorescence assay used. Docking studies by molecular modeling predicted that PMS1077 might interact directly with the IkappaB kinase-beta (IKK-beta) subunit. These results suggested that PMS1077 might suppress the activation of NF-kappaB by targeting IKK-beta involved in the NF-kappaB signaling pathway. Finally, we showed that PMS1077 sensitized cells to TNF-alpha induced apoptosis by suppressing the expression of NF-kappaB regulated anti-apoptotic genes. Our results reveal a novel function of PMS1077 on the NF-kappaB signaling pathway and imply that PMS1077 can be considered as an anti-tumor lead compound.

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TÍTULO / TITLE: - Stage-specific embryonic antigen-1 expression by undifferentiated spermatogonia in the pre-pubertal boar testis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Kim YH; Kim BJ; Kim BG; Lee YA; Kim KJ; Chung HJ; Hwang S; Woo JS; Park JK; Schmidt JA; Pang MG; Ryu BY


RESUMEN / SUMMARY: - The objective of this study was to use fluorescence-activated cell sorting (FACS) and spermatogonial stem cell (SSC) xenotransplantation to identify cell surface markers of putative porcine SSCs. Analysis of porcine testis cells enriched for spermatogonia using FACS indicated that nearly half of stage-specific embryonic antigen-1 (SSEA-1) expressing testis cells expressed the undifferentiated spermatogonia marker protein gene product 9.5 (PGP 9.5), whereas significantly fewer (P < 0.05) cells selected for Thy1, CD9 or other SSC markers expressed PGP 9.5. Immunocytochemical analysis indicated that promyelocytic leukemia zinc finger (PLZF) protein, and germ cell lineage marker VASA were expressed by SSEA-1 protein.
expressing germ cells. Spermatogonial stem cell xenotransplantation of testis cell populations enriched for cells expressing SSEA-1 generated significantly (P < 0.05; greater than 15-fold) more colonies of donor derived germ cells than unselected testis cells. In conclusion, these data indicate that SSC markers identified in rodents are likely not entirely conserved in pigs, and that SSEA-1 is a marker for porcine undifferentiated spermatogonia including SSCs in prepubertal boars and its expression may serve as a target for the further study of porcine germ cells.

[1173]

TÍTULO / TITLE: - Impact of Age at Diagnosis on Outcomes in Men with Castrate-Resistant Prostate Cancer (CRPC).
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Humphreys MR; Fernandes KA; Sridhar SS
INSTITUCIÓN / INSTITUTION: - 1. Division of Medical Oncology, British Columbia Cancer Agency, Vernon, BC, Canada;
RESUMEN / SUMMARY: - Background: The association between age and outcomes in men with castrate resistant prostate cancer (CRPC) is not well understood. Objective: We aimed to evaluate CRPC patients to determine if their age at initial diagnosis impacted their cancer specific outcomes. Design, Setting, and Participants: A retrospective chart review was conducted on 333 consecutive CRPC patients treated at the Princess Margaret Hospital (PMH) between 1995 and 2005. Patients were divided into 4 age categories, (A) <55, (B) 55-64, (C) 65-74 (reference), and (D) >/= 75 years (yrs). Outcome Measurements and Statistical Analysis: Primary endpoints included impact of age at diagnosis on overall survival (OS) and on prostate cancer specific survival. Secondary endpoints were time from diagnosis to development of CRPC, time from CRPC to death, and time from diagnosis to bone metastases. Results and Limitations: The median OS from diagnosis to death was: Group A 5.5 yrs (95% CI 3.0-7.5); Group B 6.7 yrs (95% CI 5.9-8.4); Group C 7.8 yrs (95% CI 6.6-9.3); and Group D 4.3 years (95% CI 2.9-5.0). The hazard ratio (HR) for death in Group D was 2.58 (95% CI 1.58-4.21, p=0.0002); and in Group A was 1.49 (95% CI 0.90-2.46, p=0.13). The duration of hormone sensitivity in Group D was less and predictive of OS, as was Gleason Score >/=8 and Stage 4 disease at diagnosis. Conclusions: Age at initial diagnosis appears to impact on outcome of patients who subsequently develop CRPC with a bimodal distribution of risk, with the shortest survivals in the >/=75 and <55 groups.

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Acquired resistance to zoledronic acid and the parallel acquisition of an aggressive phenotype are mediated by p38-MAP kinase activation in prostate cancer cells.

The nitrogen-containing bisphosphonates (N-BP) zoledronic acid (ZOL) inhibits osteoclast-mediated bone resorption, and it is used to prevent skeletal complications from bone metastases. ZOL has also demonstrated anticancer activities in preclinical models and, recently, in cancer patients, highlighting the interest in determining eventual mechanisms of resistance against this agent. In our study, we selected and characterised a resistant subline of prostate cancer (PCa) cells to better understand the mechanisms, by which tumour cells can escape the antitumour effect of ZOL. DU145R80-resistant cells were selected in about 5 months using stepwise increasing concentrations of ZOL from DU145 parental cells. DU145R80 cells showed a resistance index value of 5.5 and cross-resistance to another N-BP, pamidronate, but not to the non-nitrogen containing BP clodronate. Notably, compared with DU145 parental cells, DU145R80 developed resistance to apoptosis and anoikis, as well as overexpressed the anti-apoptotic protein Bcl-2 and oncoprotein c-Myc. Moreover, DU145R80 cells underwent epithelial to mesenchymal transition (EMT) and showed increased expression of the metalloproteases MMP-2/9, as well as increased invading capability. Interestingly, compared with DU145, DU145R80 cells also increased the gene expression and protein secretion of VEGF and the cytokines Eotaxin-1 and IL-12. At the molecular level, DU145R80 cells showed strong activation of the p38-MAPK-dependent survival pathway compared with parental sensitive cells. Moreover, using the p38-inhibitor SB203580, we completely reversed the resistance to ZOL, as well as EMT marker expression and invasion. Furthermore, SB203580 treatment reduced the expression of VEGF, Eotaxin-1, IL-12, MMP-9, Bcl-2 and c-Myc. Thus, for the first time, we demonstrate that the p38-MAPK pathway can be activated under continuous extensive exposure to ZOL in PCa cells and that the p38-MAPK pathway has a critical role in the induction of resistance, as well as in the acquisition of a more aggressive and invasive phenotype.
Magnetic resonance imaging for prostate cancer clinical application.

As prostate cancer is a biologically heterogeneous disease for which a variety of treatment options are available, the major objective of prostate cancer imaging is to achieve more precise disease characterization. In clinical practice, magnetic resonance imaging (MRI) is one of the imaging tools for the evaluation of prostate cancer, the fusion of MRI or dynamic contrast-enhanced MRI (DCE-MRI) with magnetic resonance spectroscopic imaging (MRSI) is improving the evaluation of cancer location, size, and extent, while providing an indication of tumor aggressiveness. This review summarizes the role of MRI in the application of prostate cancer and describes molecular MRI techniques (including MRSI and DCE-MRI) for aiding prostate cancer management.

Comparable effect with minimal morbidity of low-dose Tokyo 172 strain compared with regular dose Connaught strain as an intravesical bacillus Calmette-Guerin prophylaxis in nonmuscle invasive bladder cancer: Results of a randomized prospective comparison.

AIM: The aim was to compare patients’ morbidity and response of bacillus Calmette-Guerin (BCG) prophylaxis after the intravesical instillation of low-dose Tokyo 172 strain and regular dose Connaught strain in patients with nonmuscle invasive bladder cancer (NMIBC). PATIENTS AND METHODS: This was a randomized, active-controlled, open-label, monocenter study. Thirty-eight, NMIBC patients were treated sequentially, in a random
order, with low-dose Tokyo 172 strain and regular dose Connaught strain, receiving each therapy for 6 weeks. A total of 18 and 20 patients were randomly assigned to a Tokyo 172 strain arm and a Connaught strain arm, respectively. Complication, morbidity, and recurrence-free survival (RFS) after each treatment were compared. RESULTS: There was no significant difference in the 1-year RFS rate in patients treated with Tokyo 172 strain and Connaught strain (72.2% vs. 83.5%, respectively; P = 0.698). There were no significant differences in adverse events between the arms. Severe adverse events (>Grade 3) were seen in 15% of the Connaught strain group while no severe adverse events were observed as a result of Tokyo 172 strain. CONCLUSION: Our results indicated that low-dose Tokyo 172 strain decreased adverse events although it was not significant, and the RFS difference was not statistically significant between the two arms. Further investigation is warranted.

[1177]

TÍTULO / TITLE: - RANKL/RANK/MMP-1 Molecular Triad Contributes to the Metastatic Phenotype of Breast and Prostate Cancer Cells In Vitro.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago)

1371/journal.pone.0063153

AUTORES / AUTHORS: - Casimiro S; Mohammad KS; Pires R; Tato-Costa J; Alho I; Teixeira R; Carvalho A; Ribeiro S; Lipton A; Guise TA; Costa L

INSTITUCIÓN / INSTITUTION: - Clinical and Translational Oncology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina de Lisboa, Lisbon, Portugal; Histology Unit, Instituto de Medicina Molecular, Faculdade de Medicina de Lisboa, Lisbon, Portugal.

RESUMEN / SUMMARY: - The osteolytic nature of bone metastasis results from a tumor-driven increased bone resorption. Bone remodeling is orchestrated by the molecular triad RANK-RANKL-OPG. This process is dysregulated in bone metastases, mostly via induction of RANKL by tumor-derived factors. These factors increase expression of RANKL, which induce osteoclast formation, function, and survival, thereby increasing bone resorption. RANK is unexpectedly expressed by cancer cells, and the activation of RANKL-RANK pathway correlates with an increased invasive phenotype. To investigate the interaction between RANK expression in human breast and prostate cancer cells and their pro-metastatic phenotype we analyzed the activation of RANKL-RANK pathway and its effects on cell migration, invasion, gene expression in vitro, and osteolysis-inducing ability in vivo. RANKL activates kinase signaling pathways, stimulates cell migration, increases cell invasion, and up-regulates MMP-1 expression. In vivo, MMP-1 knockdown resulted in smaller x-ray osteolytic lesions and osteoclastogenesis, and decreased tumor burden.
Therefore, RANKL inhibition in bone metastatic disease may decrease the levels of the osteoclastogenesis inducer MMP-1, contributing to a better clinical outcome.

[1178]

**TÍTULO / TITLE:** - Influence of concurrent medications on outcomes of men with prostate cancer included in the TAX 327 study.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 5489/cuaj.267

**AUTORES / AUTHORS:** - Niraula S; Pond G; de Wit R; Eisenberger M; Tannock IF; Joshua AM

**INSTITUCIÓN / INSTITUTION:** - Division of Medical Oncology, Princess Margaret Hospital/University of Toronto, Toronto, ON;

**RESUMEN / SUMMARY:** - OBJECTIVES: The TAX 327 trial was pivotal in establishing docetaxel in castration refractory metastatic prostate cancer. Various commonly prescribed and over-the-counter co-administered medications are thought to exhibit anti-neoplastic properties and/or could potentially have pharmacokinetic interactions with docetaxel lessening the effectiveness of chemotherapy. METHODS: To examine the effect of on prostate cancer outcomes within this trial, we examined overall survival, prostate-specific antigen (PSA) response, percent PSA reduction, pain response and QOL responses for 14 families of medications including metformin, digoxin, verapamil, proton pump inhibitors, nitrates, statins, cox-2 inhibitors, warfarin, heparins, ascorbic acid, selenium, tocopherol, antidepressants and erythropoietin. RESULTS: Our findings did not reveal any medication that had a significant additive or synergistic effect with docetaxel. We did note, however, that patients on digoxin or verapamil had poorer overall survival, possibly due to a trend of fewer cycles of administered chemotherapy being administered to the verapamil group, consistent with a pharmacokinetic interaction. CONCLUSIONS: These data are only hypothesis-generating given the statistical limitations, but may form a basis for similar future analysis in other malignancies. The data suggest the need to be aware of pharmacokinetic interactions with medications that may interact with docetaxel.

[1179]

**TÍTULO / TITLE:** - Survival after a diagnosis of testicular germ cell cancers in Germany and the United States, 2002-2006: A high resolution study by histology and age.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

Introduction: The aim of this study was to provide detailed age-specific (5-year age groups) and histology-specific (histologic subtypes of seminoma and nonseminoma) relative survival estimates of testicular germ cell cancer patients in Germany and the United States (U.S.) for the years 2002-2006 and to compare these estimates between countries. Methods: We pooled data from 11 cancer registries of Germany and used data from the U.S. (SEER-13 database) including 11,508 and 10,774 newly diagnosed cases (1997-2006) in Germany and the U.S., respectively. We estimated 5-year relative survival (5-year-RS) by histology and age based on period analysis. Results: 5-year-RS for testicular germ cell tumors was 96.7% and 96.3% in Germany and the U.S., respectively. 5-Year-RS for spermatocytic seminoma was close to 100% in both countries. 5-Year-RS for nonseminoma was lower than for classical seminoma in Germany (93.3% versus 97.6%) and the U.S. (91.0% versus 98.2%). Among nonseminomas, choriocarcinomas provided the lowest 5-year-RS in both countries (Germany 80.1%, U.S. 79.6%). Age-specific 5-year-RS for seminoma showed only little variation by age. 5-Year-RS for nonseminomas tended to be lower at higher ages, especially for malignant teratoma. Discussion: This is the first study that provides up-to-date survival estimates for testicular cancer by histology and age in Germany and the U.S. Survival after a diagnosis of testicular cancer is very comparable between Germany and the U.S. 5-Year-RS for spermatocytic seminoma was close to 100% and the lowest 5-year-RS occurred among choriocarcinoma. Higher age at diagnosis is associated with a poorer prognosis among nonseminoma patients.
AUTORES / AUTHORS: - Gao T; He B; Pan Y; Li R; Xu Y; Chen L; Nie Z; Gu L; Wang S
INSTITUCIÓN / INSTITUTION: - Central Laboratory, Nanjing First Hospital, Nanjing Medical University, Nanjing, Jiangsu, China.
RESUMEN / SUMMARY: - The retinoic acid receptor beta2 (RARbeta2) is a type of nuclear receptor that is activated by both all-trans retinoic acid and 9-cis retinoic acid, which has been shown to function as a tumor suppressor gene in different types of human tumors. Previous reports demonstrated that the frequency of RARbeta2 methylation was significantly higher in prostate cancer patients compared with controls, but the relationship between RARbeta2 promoter methylation and pathological stage or Gleason score of prostate cancer remained controversial. Therefore, a meta-analysis of published studies investigating the effects of RARbeta2 methylation status in prostate cancer occurrence and association with both pathological stage and Gleason score in prostate cancer was performed in the study. A total of 12 eligible studies involving 777 cases and 404 controls were included in the pooled analyses. Under the random-effects model, the pooled OR of RARbeta2 methylation in prostate cancer patients, compared to non-cancer controls, was 17.62 with 95%CI = 6.30-49.28. The pooled OR with the fixed-effects model of pathological stage in RASSF1A methylated patients, compared to unmethylated patients, was 0.67 (95%CI = 0.40-1.09) and the pooled OR of low-GS in RARbeta2 methylated patients by the random-effect model, compared to high-GS RARbeta2 methylated patients, was 0.54 (95%CI = 0.28-1.04). This study showed that RARbeta2 might be a potential biomarker in prostate cancer prevention and diagnosis. The detection of RARbeta2 methylation in urine or serum is a potential non-invasive diagnostic tool in prostate cancer. The present findings also require confirmation through adequately designed prospective studies.

[1181]
TÍTULO / TITLE: - Tumor suppressive miR-509-5p contributes to cell migration, proliferation and antiapoptosis in renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1007/s11845-013-0941-y
AUTORES / AUTHORS: - Zhang WB; Pan ZQ; Yang QS; Zheng XM
INSTITUCIÓN / INSTITUTION: - Department of Urology, Zhongnan Hospital, Wuhan University, 169 Donghu Road, Wuhan, China, zhangweibin1969@163.com.
RESUMEN / SUMMARY: - PURPOSE: The aim of this study was to determine the expression and function of miR-509-5p in renal cell carcinoma (RCC).
MATERIALS AND METHODS: In this research, we have conducted quantitative real-time polymerase chain reaction (qRT-PCR) assay to determine the
expression level of miR-509-5p in tissues and plasma from renal cell carcinoma patients. We preformed in vitro migration scratch assay, flow cytometry analysis and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay to determine the exact function of miR-509-5p. RESULTS: We evaluated the expression level of miR-509-5p in RCC tissues and paired adjacent normal tissues from 42 patients and found that miR-509-5p expression in 42 RCC specimens was significantly down-regulated compared to that in adjacent normal tissue. Furthermore, the level of miR-509-5p in RCC patients’ plasma was significantly lower than that in control plasma. In addition, the overexpression of miR-509-5p suppressed the proliferation of RCC cell (786-0), induced cell apoptosis and inhibited cell migration in vitro. CONCLUSION: In this study, we have shown that miR-509-5p played an important role in RCC by inhibiting cell proliferation and migration and by promoting cell apoptosis. In addition, miR-509-5p expression was significantly lower in RCC patient plasma compared to that in normal individuals.

[1182]

**TÍTULO / TITLE:** Impact of renal artery stenting on cytokine levels, left ventricle mass and diastolic function.

**RESUMEN / SUMMARY:**

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Rzeznik D; Przewlocki T; Kablak-Ziembicka A; Raslawiecka A; Kozanecki A; Lach J; Podolec P

**INSTITUCIÓN / INSTITUTION:** Department of Cardiac and Vascular Diseases, Institute of Cardiology, Jagiellonian University School of Medicine, The Pope John Paul II Hospital, Krakow, Poland. rzeznikd@poczta.onet.pl

**RESUMEN / SUMMARY:** BACKGROUND: Significant renal artery stenosis (RAS) may lead to left ventricle (LV) hypertrophy and diastolic function (DF) impairment through complex mechanisms: activation of cytokines and/or systolic and diastolic blood pressure (SBP, DBP) increase. AIM: To assess interrelations between LV mass (LVM), DF and cytokines in patients undergoing renal artery stenting (PTA, percutaneous angioplasty of renal artery). METHODS: The study group comprised 72 subjects (44.4% men), 64.1 +/- 9.9 years with RAS referred to PTA. SBP, DBP, transforming growth factor beta1 (TGF-beta1), aldosterone, B-type natriuretic peptide (BNP) levels and change in LVM and LVM index (LVMi) and DF (E(vel), e'(vel), E/A ratio, E/e' ratio, Ar(time)-A(time)) on echocardiography were assessed preprocedurally, and three and 12 months postprocedurally. RESULTS: TGF-beta1 level decreased from 13.3 +/- 14.9 to 8.6 +/- 8.0 ng/mL (p = 0.027), while BNP increased from 89.1 +/- 86.3 to 131 +/- 105 pmol/mL (p < 0.001). A significant
reduction in LVMI in women (79.4 +/- 16.9 vs. 95.7 +/- 18.5 g/m(2), p < 0.001) and men (77.2 +/- 16.8 vs. 100.1 +/- 19.7 g/m(2), p < 0.001) was found at 12 months vs. baseline. Degree of LVM reduction correlated with baseline LVM (p < 0.001; r = -0.612) and e'(vel) (p = 0.05; r = 0.230), but not with BP values. Among DF parameters, only e'(vel) increased significantly at 12 months (5.54 +/- 1.57 vs. 5.92 +/- 1.65 cm/s; p = 0.039), while A/E and E/e' ratio, Ar(time)-A(time) remained similar (p = 0.457, p = 0.283 and p = 0.258). Factors associated with e'(vel) increase >/= 0.3 cm/s at 12 months were baseline LVM < 165 g (p = 0.043, RR = 1.39, CI 1.01-1.46), E(vel) (p = 0.015, RR = 1.26, CI 1.15-1.52), e'(vel) (p < 0.001, RR = 1.42, CI 1.18-1.7), DBP decrease > 10 mm Hg (p = 0.055, RR = 1.2, CI 1.0-1.44) and TGF-beta1 > 8 ng/mL (p = 0.024, RR = 1.24, CI 1.03-1.49) at 12 months. CONCLUSIONS: Significant LVMI reduction was observed after PTA of RAS, but it was independent of BP reduction. e'(vel) increase was independently associated with baseline LVM, E(vel), e'(vel), and 12 month decrease in DBP > 10 mm Hg.

[1183]

TÍTULO / TITLE: - Comparative proteomics analysis of sodium selenite-induced apoptosis in human prostate cancer cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Chen P; Wang L; Li N; Liu Q; Ni J

INSTITUCIÓN / INSTITUTION: - College of Life Sciences, Shenzhen Key Laboratory of Microbial Genetic Engineering, Shenzhen University, Shenzhen, Guangdong, P.R. China. jznl@szu.edu.cn.

RESUMEN / SUMMARY: - Selenium is an important trace mineral necessary for human health. Clinical trials have shown potential inhibitory effects of selenium in advanced or aggressive prostate cancer. However, its mechanism of action remains unclear. This study investigated the mechanism of action of sodium selenite in human prostate cancer PC-3 cells using proteomics. CCK-8 assays were used to detect cell viability and the inhibitory rate. Cell apoptosis was detected by annexin V-FITC and propidium iodide double staining using flow cytometry. Selenite inhibited the growth of PC-3 cells causing them to display morphological changes typical of apoptosis. The rate of cell apoptosis also increased. Proteomics identified a variety of differentially expressed proteins in PC-3 cells exposed to selenite. Eighteen protein spots were identified by MALDI-TOF mass spectrometry. These proteins were separated into those involved in redox balance, protein degradation and cellular energy metabolism. Three differently expressed proteins (SOD1, Stathmin and Erp29) were chosen for Western blot verification, together with several apoptosis-related proteins.
Western blot analyses showed that selenite-induced apoptosis was accompanied by activation of caspase-8 and specific proteolytic cleavage of PARP. This led to an increase in the pro-apoptotic protein Bax, and to a decrease in the anti-apoptotic protein Bcl-2 and in hypoxia inducible factor-1alpha. Increased ROS generation and decreased mitochondrial membrane potential were consistent with reduced expression of antioxidative proteins identified by comparative proteomics. We therefore propose that sodium selenite induces the apoptosis of PC-3 cells mainly through the mitochondrial pathway, but also via ER stress and HIF-1alpha mediated pathways.

[1184]

**Título / Title:** Tetrandrine triggers apoptosis and cell cycle arrest in human renal cell carcinoma cells.

**Resumen / Summary:** Tetrandrine is a cytotoxic compound capable of exerting remarkable antitumor activity against many cancer cells in vitro and in vivo. However, little is known about its effect on human renal cell carcinoma (RCC). In the present study, using RCC 786-O, 769-P and ACHN cell lines as the model system, we demonstrated the anticancer effect of tetrandrine against RCC and clarified its underlying mechanisms. Tetrandrine treatment showed growth inhibitory effects on RCC cells in a time- and dose-dependent manner. Additionally, flow cytometric studies revealed that tetrandrine was capable of inducing G1 cell cycle arrest and apoptosis in RCC cells. Mechanically, activation of caspase-8, caspase-9, and caspase-3 and increasing expression of cell cycle regulatory protein p21WAF1/CIP1 and p27KIP1 were observed in tetrandrine-treated RCC cells. This study provides the first evidence that tetrandrine triggered apoptosis and cell cycle arrest in RCC 786-O, 769-P and ACHN cells in vitro; these events are associated with caspase cascade activation and upregulation of p21 and p27. Our results thus provide rational evidence supporting the application of tetrandrine as a novel therapeutic agent against RCC in the clinical setting.

[1185]

**Título / Title:** M-ds-P21 induces cell apoptosis in bladder cancer T24 cells through P53 independent pathway.

**Resumen / Summary:**

AUTORES / AUTHORS: - Wang H; Liu W; Jin J; Zhou L; Liang L; Guo Y

INSTITUCIÓN / INSTITUTION: - Department of Urology, Peking University First Hospital and Institute of Urology, Peking University, National Research Center for Genitourinary Oncology, Beijing, China.

RESUMEN / SUMMARY: - OBJECTIVES: To investigate the effect of M-ds-P21 on the apoptosis of bladder cancer T24 cells and its potential mechanism. MATERIALS AND METHODS: Effect of M-ds-P21 on T24 cells were assessed by cell morphology and Western blot. Apoptosis was quantified by Annexin-V flow-cytometry analysis. To uncover the role of P53 in M-ds-P21-mediated apoptosis of T24 cells, we knocked down P53 before treating cells with M-ds-P21, and then assayed P21 and apoptosis-related protein by Western blot. To uncover the mechanism by which M-ds-P21 played stronger effect than ds-P21, we performed confocal microscope analyses. RESULTS: Both M-ds-P21 and ds-P21 treatment changed the cell morphology, leading to cell apoptosis after 3 days. Apoptosis induced by M-ds-P21 and ds-P21 treatment is not P53-dependent but caspase-dependent. Compared with ds-P21, M-ds-P21 significantly increased the bioavailability of ds-RNA in T24 cells. CONCLUSIONS: M-ds-P21 treatment induces more apoptotic population than ds-P21 does. The mechanism for stronger effect of M-ds-P21 is partly due to the enhanced bioavailability of ds-RNA in human bladder cancer T24 cells, and not P53-dependent but caspase-dependent.

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[1186]

TÍTULO / TITLE: - Inverted variant of urothelial carcinoma of the urinary bladder: a report of three cases and a proposal for a new clinicopathologic entity.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Terada T

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Shizuoka City Shimizu Hospital, Shizuoka, Japan. piyo0111jp@yahoo.co.jp

RESUMEN / SUMMARY: - Inverted urothelial carcinoma (UC) without papillary areas is very rare; only 31 cases of three papers have been reported. The author herein reports three additional cases, and proposes the term “inverted variant” (IV) of UC. The materials were 3 cases of IV of UC, 5 cases of inverted papilloma (IP), and two cases of nested variant (NV) of UC. The three cases of IV of UC consisted of 56-year-old woman, 63-year-old man, and 78-year-old man. Presenting symptoms were hematuria in all cases. The cystoscopic findings were elevated tumors without papillary proliferations in all cases. The treatment was transurethral tumor resection (TUR-BT) in all cases. The sizes
was 0.6 cm, 0.5 cm, and 3 cm. Microscopically, IV of UC showed inverted growth of atypical cells without papillary proliferations. Compared to IP, the inverted growth pattern was similar, but cytological atypia and thick trabeculae were noted in IV of UP while they were absent in IP. Compared to NV of UC, the growth pattern is different; NV of UC showed nested and vague tubular pattern. The cellular atypia is more pronounced in IV of UC than NV of UC. Immunohistochemically, p53 expression was seen in all the cases of IV of UC and in all the cases of NV of UC, while p53 expression was negative in all the cases of IP. Ki-67 labeling index was 25, 30 and 40% in IV of UC, 15 and 30% in NV of UC, and 3, 5, 6, 7, 9% in IP. Invasive features were seen in 1 case of IV of UC and 2 cases of NV of UC. In all cases of IV of UC, IP, and NV of UC, the TUR-BT, but one case of IV of UC, showed no recurrence after TUR-BT, while one case of IV of UC showed a recurrence. In conclusion, the IV and UC were structurally and cytologically very different from the NV of UC. The IV of UC was structurally similar to IP, but cellular atypia and thickened trabeculae were seen in IV and UC. p53 expression and Ki-67 labeling status were entirely different between in IV of UC and IP. The author proposes the term of IV of UC as a new clinicopathological entity.

[1187]

TÍTULO / TITLE: - Genome-wide testing of putative functional exonic variants in relationship with breast and prostate cancer risk in a multiethnic population.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Haiman CA; Han Y; Feng Y; Xia L; Hsu C; Sheng X; Pooler LC; Patel Y; Kolonel LN; Carter E; Park K; Le Marchand L; Van Den Berg D; Henderson BE; Stram DO
INSTITUCIÓN / INSTITUTION: - Department of Preventive Medicine, Keck School of Medicine and Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, California, United States of America. haiman@usc.edu
RESUMEN / SUMMARY: - Rare variation in protein coding sequence is poorly captured by GWAS arrays and has been hypothesized to contribute to disease heritability. Using the Illumina HumanExome SNP array, we successfully genotyped 191,032 common and rare non-synonymous, splice site, or nonsense variants in a multiethnic sample of 2,984 breast cancer cases, 4,376 prostate cancer cases, and 7,545 controls. In breast cancer, the strongest associations included either SNPs in or gene burden scores for genes LDLRAD1, SLC19A1, FGFBP3, CASP5, MMAB, SLC16A6, and INS-IGF2. In prostate cancer, one of the most associated SNPs was in the gene GPRC6A (rs2274911, Pro91Ser, OR = 0.88, P = 1.3 x 10(-5)) near to a known risk locus
for prostate cancer; other suggestive associations were noted in genes such as F13A1, ANXA4, MANSC1, and GP6. For both breast and prostate cancer, several of the most significant associations involving SNPs or gene burden scores (sum of minor alleles) were noted in genes previously reported to be associated with a cancer-related phenotype. However, only one of the associations (rs145889899 in LDLRAD1, \( p = 2.5 \times 10^{-7} \) only seen in African Americans) for overall breast or prostate cancer risk was statistically significant after correcting for multiple comparisons. In addition to breast and prostate cancer, other cancer-related traits were examined (body mass index, PSA level, and alcohol drinking) with a number of known and potentially novel associations described. In general, these findings do not support there being many protein coding variants of moderate to high risk for breast and prostate cancer with odds ratios over a range that is probably required for protein coding variation to play a truly outstanding role in risk heritability. Very large sample sizes will be required to better define the role of rare and less penetrant coding variation in prostate and breast cancer disease genetics.

[1188]

**TÍTULO / TITLE:** Gene expression study related with the intrinsic pathway of apoptosis in bladder cancer by real-time PCR technique.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Barione DF; Lizarte FS; Novais PC; de Carvalho CA; Valeri FC; Peria FM; de Oliveira HF; Zanette DL; Silva WA Jr; Cologna AJ; Reis RB; Tucci S Jr; Martins AC; Tirapelli DP; Tirapelli LF

**INSTITUCION / INSTITUTION:** Departamento de Cirurgia e Anatomia, Faculdade de Medicina de Ribeirao Preto, Universidade de Sao Paulo, Ribeirao Preto, SP, Brasil.

**RESUMEN / SUMMARY:** We examined the expression of anti-apoptotic genes (XIAP and Bcl-2) and apoptotic genes (cytochrome c, caspase-9, Apaf-1) in tissue samples of patients with superficial bladder cancer. Thirty-two bladder cancer tissue samples (8 papillary urothelial neoplasm of low malignant potential, 10 low-grade, and 14 high-grade) and 8 normal bladder tissue samples from necropsy were used for the study of gene expression by real-time PCR analysis. Analysis of the expression of apoptotic gene constituents of an apoptosome demonstrated an increase in Apaf-1 expression in the three tumor grades when compared with the control (\( P < 0.01 \), \( P < 0.05 \), and \( P < 0.01 \)), low expression of caspase-9 in all groups (\( P < 0.05 \)), and an increase in cytochrome c expression in all tumor grades in relation to the control, although without statistically significant difference. The expression of anti-apoptotic genes revealed an increase in XIAP expression in all tumor grades in relation
to the control, although without statistically significant difference, and low expression of Bcl-2 in all tumor grades and the control (P < 0.05). The results proved that there is low evidence of apoptotic activity by the intrinsic pathway, demonstrated by the low expression of caspase-9 and considerable increase in XIAP expression, which may render these genes potential therapeutic targets in bladder cancer treatment.

[1189]
**TÍTULO / TITLE:** - Expanding Utilization of Intensity-Modulated Radiotherapy for Prostate Cancer: Comment on “Comparative Effectiveness of Intensity-Modulated Radiotherapy and Conventional Conformal Radiotherapy in the Treatment of Prostate Cancer After Radical Prostatectomy”

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](http://jama.ama-assn.org/search.dtl)

**REVISTA / JOURNAL:** - JAMA. Acceso gratuito al texto completo.

- Enlace al texto completo (gratuito o de pago) [1001/jamainternmed.2013.6755](1001/jamainternmed.2013.6755)

**AUTORES / AUTHORS:** - Cooperberg MR

[1190]
**TÍTULO / TITLE:** - Preclinical analyses of intravesical chemotherapy for prevention of bladder cancer progression.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](http://jama.ama-assn.org/search.dtl)

**REVISTA / JOURNAL:** - Oncotarget. 2013 Feb;4(2):269-76.

**AUTORES / AUTHORS:** - Delto JC; Kobayashi T; Benson M; McKiernan J; Abate-Shen C

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Columbia University Medical Center, New York, NY, USA.

**RESUMEN / SUMMARY:** - There is a critical need to identify treatment options for patients at high risk for developing muscle invasive bladder cancer that avoid surgical removal of the bladder (cystectomy). In the current study, we have performed preclinical studies to investigate the efficacy of intravesical delivery of chemotherapy for preventing progression of bladder cancer. We evaluated three chemotherapy agents, namely cisplatin, gemcitabine, and docetaxel, which are currently in use clinically for systemic treatment of muscle invasive bladder cancer and/or have been evaluated for intravesical therapy. These preclinical studies were done using a genetically-engineered mouse (GEM) model that progresses from carcinoma in situ (CIS) to invasive, metastatic bladder cancer. We performed intravesical treatment in this GEM model using cisplatin, gemcitabine, and/or docetaxel, alone or by combining two agents, and evaluated whether such treatments inhibited progression to invasive, metastatic...
bladder cancer. Of the three single agents tested, gemcitabine was most effective for preventing progression to invasive disease, as assessed by several relevant endpoints. However, the combinations of two agents, and particularly those including gemcitabine, were more effective for reducing both tumor and metastatic burden. Our findings suggest combination intravesical chemotherapy may provide a viable bladder-sparing treatment alternative for patients at high risk for developing invasive bladder cancer, which can be evaluated in appropriate clinical trials.

[1191]
TÍTULO / TITLE: - Urachal carcinoma.
RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)
AUTORES / AUTHORS: - Abeygunasekera AM; Ranasinghe DD
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[1192]
TÍTULO / TITLE: - Activation of NF-kappa B signaling promotes growth of prostate cancer cells in bone.
RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)
AUTORES / AUTHORS: - Jin R; Sterling JA; Edwards JR; DeGraff DJ; Lee C; Park SI; Matusik RJ
INSTITUCIÓN / INSTITUTION: - Vanderbilt Prostate Cancer Center and Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, Tennessee, USA. [renejie.jin@vanderbilt.edu](mailto:renejie.jin@vanderbilt.edu)
RESUMEN / SUMMARY: - Patients with advanced prostate cancer almost invariably develop osseous metastasis. Although many studies indicate that the activation of NF-kappaB signaling appears to be correlated with advanced cancer and promotes tumor metastasis by influencing tumor cell migration and angiogenesis, the influence of altered NF-kappaB signaling in prostate cancer cells within boney metastatic lesions is not clearly understood. While C4-2B and PC3 prostate cancer cells grow well in the bone, LNCaP cells are difficult to grow in murine bone following intraskeletal injection. Our studies show that when compared to LNCaP, NF-kappaB activity is significantly higher in C4-2B and PC3, and that the activation of NF-kappaB signaling in prostate cancer cells resulted in the increased expression of the osteoclast inducing genes PTHrP and RANKL. Further, conditioned medium derived from NF-kappaB activated
LNCaP cells induce osteoclast differentiation. In addition, inactivation of NF-kappaB signaling in prostate cancer cells inhibited tumor formation in the bone, both in the osteolytic PC3 and osteoblastic/osteoclastic mixed C4-2B cells; while the activation of NF-kappaB signaling in LNCaP cells promoted tumor establishment and proliferation in the bone. The activation of NF-kappaB in LNCaP cells resulted in the formation of an osteoblastic/osteoclastic mixed tumor with increased osteoclasts surrounding the new formed bone, similar to metastases commonly seen in patients with prostate cancer. These results indicate that osteoclastic reaction is required even in the osteoblastic cancer cells and the activation of NF-kappaB signaling in prostate cancer cells increases osteoclastogenesis by up-regulating osteoclastogenic genes, thereby contributing to bone metastatic formation.

[1193]
TÍTULO / TITLE: - Evaluation of Serum Calcium as a Predictor of Biochemical Recurrence following Salvage Radiation Therapy for Prostate Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Peterson JL; Buskirk SJ; Heckman MG; Parker AS; Diehl NN; Tzou KS; Paryani NN; Ko SJ; Daugherty LC; Vallow LA; Pisansky TM
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Mayo Clinic Florida, Jacksonville, FL 32224, USA.
RESUMEN / SUMMARY: - Background. Previous reports have shown a positive association between serum calcium level and prostate cancer mortality. However, there is no data regarding whether higher serum calcium levels are associated with increased risk of biochemical recurrence (BCR) following salvage radiation therapy (SRT) for prostate cancer. Herein, we evaluate the association between pretreatment serum calcium levels and BCR in a cohort of men who underwent SRT. Methods. We evaluated 165 patients who underwent SRT at our institution. Median dose was 65.0 Gy (range: 54.0-72.4 Gy). We considered serum calcium as both a continuous variable and a 3-level categorical variable (low [<9.0 mg/dL], moderate [9.0 mg/dL and <=9.35 mg/dL], and high [>9.35 mg/dL]) based on sample tertiles. Results. We observed no evidence of a linear association between serum calcium and BCR (relative risk (RR): 0.96, P = 0.76). Compared to men with low calcium, there was no significantly increased risk of BCR for men with moderate (RR: 0.94, P = 0.79) or high (RR: 1.08, P = 0.76) serum calcium levels. Adjustment for clinical, pathological, and SRT characteristics in multivariable analyses did not alter these findings. Conclusion. Our results provide evidence that pretreatment serum calcium is unlikely to be a useful tool in predicting BCR risk following SRT.
TÍTULO / TITLE: - Chemotherapy for prostate cancer: Clinical practice in Canada.
RESUMEN / SUMMARY: -  
AUTORES / AUTHORS: - Saad F; Asselah J
INSTITUCIÓN / INSTITUTION: - Chairman, National Cancer Institute of Canada Clinical Trials Genitourinary Group (NCIC-CTG G-U) and Canadian Urologic Oncology Group (CUOG); Professor and Chief of Urology, Director of Urologic Oncology, Endowed Chair in Prostate Cancer, Centre Hospitalier de l'Universite de Montreal, Montreal, QC.
RESUMEN / SUMMARY: - Whereas prostate cancer was once deemed unresponsive to chemotherapy, there is now evidence that patients with metastatic castration-resistant prostate cancer can obtain a survival benefit from both first-line (docetaxel-based) and second-line (cabazitaxel-based) chemotherapy. The side effects of these agents have been shown to be predictable and manageable, particularly in North American centres. However, patient selection remains a key issue, with the aim of delivering each line of treatment at a time when the individual patient remains fit and well enough to tolerate a cytotoxic regimen. Hence, it is increasingly important for urologists and oncologists to work together to ensure timely consideration of the chemotherapeutic approach before it is precluded by a decline in performance status.

TÍTULO / TITLE: - Holmium laser versus conventional transurethral resection of the bladder tumor.
RESUMEN / SUMMARY: -  
AUTORES / AUTHORS: - Teng JF; Wang K; Yin L; Qu FJ; Zhang DX; Cui XG; Xu DF
INSTITUCIÓN / INSTITUTION: - Department of Urology, Shanghai Changzheng Hospital, Second Military Medical University, Shanghai 200003, China. Department of Urology, General Hospital of Beijing Military Region, Beijing 100700, China.
RESUMEN / SUMMARY: - BACKGROUND: Transurethral resection of the bladder tumor (TURBT) remains the gold standard for non-muscle-invasive bladder cancer (NMIBC). Laser techniques have been widely used in urology. This analysis aimed to assess the safety and efficacy of holmium resection of the bladder tumor (HoLRBT) vs. TURBT. METHODS: A systemic search of MEDLINE, Embase, Web of Science, and The Cochrane Library as well as manual bibliography searches were performed to identify the relevant studies. The pooled estimates of operation time, obturator nerve reflex rate, bladder...
perforation rate, bladder irrigation rate, catheterization time, hospital stay, and one- and two-year recurrence free survivals were calculated. RESULTS: Five studies were enrolled into our meta-analysis. No significant difference was observed in the operation time between groups (weighted mean difference (WMD) 1.01, 95% confidential interval (95%CI) -3.52 - 5.54, P = 0.66). The significant difference in the obturator nerve reflex (OR 0.05, 95%CI 0.01 - 0.04, P = 0.004), bladder perforation (OR 0.14, 95%CI 0.03 - 0.61, P = 0.009), bladder irrigation (OR 0.13, 95%CI 0.04 - 0.45, P = 0.001), catheterization time (WMD -0.96, 95%CI -1.11 to -0.82, P < 0.00001), and hospital stay (WMD -1.46, 95%CI -1.65 to -1.27, P < 0.00001) showed advantages of HoLRBT over TURBT. The 2-year recurrence free survival rate favors the HoLRBT group (OR 1.46, 95%CI 1.02 - 2.11, P = 0.04). CONCLUSIONS: As a promising technique, HoLRBT is safe and efficient, and showed several advantages over TURBT. HoLRBT can be used as an alternative procedure for TURBT in terms of low-grade papillary urothelial carcinoma or low-grade early TNM-stage urothelial carcinoma.

[1196]

**TÍTULO / TITLE:** Potential biofluid markers and treatment targets for renal cell carcinoma.

**RESUMEN / SUMMARY:**

Enlace al Resumen / Link to its Summary


Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.52

**AUTORES / AUTHORS:** Wettersten HI; Weiss RH

**INSTITUCIÓN / INSTITUTION:** Division of Nephrology, University of California, Davis, CA 95616, USA.

**RESUMEN / SUMMARY:** Renal cell carcinoma (RCC) is the 13th most common cancer in the world and one of the few cancers for which incidence is increasing. This disease is generally asymptomatic at an early stage and is highly metastatic. Frequently discovered by physicians in the process of working up other diseases such as acute kidney injury, RCC is often discovered in an advanced form and many patients have metastases at the time of diagnosis. Given that life expectancy with currently approved therapies for metastatic RCC is approximately 1-2 years, biomarkers for RCC that will enable early detection are urgently needed. Although it is unlikely that highly sensitive and specific biomarkers will be identified in the near future that are useful for screening the general population, a noninvasive marker or set of markers could soon be used in general medicine, nephrology, and urology clinics to screen patients at increased risk of RCC. In addition to the ongoing need for RCC biomarkers, the frequent resistance reported with currently available targeted therapies makes the identification of new therapeutic targets similarly important. Many promising leads for new targeted therapies have come
to light; some of these therapies are in clinical trials and others are still being evaluated in the laboratory.

[1197]

**TÍTULO / TITLE:** - Radiation therapy modalities in prostate cancer.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** - Pugh TJ; Nguyen BN; Kanke JE; Johnson JL; Hoffman KE

**INSTITUCIÓN / INSTITUTION:** - From the Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas 77054, USA. tpugh@mdanderson.org

**RESUMEN / SUMMARY:** - Definitive radiation therapy is the preferred treatment for many men with prostate cancer. Several modalities are used for radiation treatment delivery, including 3-dimensional conformal radiation therapy, intensity-modulated radiation therapy, proton beam therapy, stereotactic body radiation therapy, high-dose-rate prostate brachytherapy, and low-dose-rate prostate brachytherapy. This article reviews technologic advances that have enhanced radiation delivery and describes contemporary radiation treatment techniques for prostate cancer.

[1198]

**TÍTULO / TITLE:** - Is small prostate volume a predictor of Gleason score upgrading after radical prostatectomy?
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**AUTORES / AUTHORS:** - Chung MS; Lee SH; Lee DH; Chung BH

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Gangnam Severance Hospital, Yonsei University Health System, 211 Eonju-ro, Gangnam-gu, Seoul 135-720, Korea. chung646@yuhs.ac.

**RESUMEN / SUMMARY:** - Purpose: We aimed to analyze the relationship between prostate volume and Gleason score (GS) upgrading [higher GS category in the radical prostatectomy (RP) specimen than in the prostate biopsy] in Korean men. Materials and Methods: We retrospectively analyzed the medical records of 247 men who underwent RP between May 2006 and April 2011 at our institution. Transrectal ultrasound (TRUS) volume was categorized as 25 cm(3) or less (n=61), 25 to 40 cm(3) (n=121) and greater than 40 cm(3) (n=65). GS was examined as a categorical variable of 6 or less, 3+4 and 4+3 or greater. The relationship between TRUS volume and upgrading of GS was analyzed using multivariate logistic regression. Results: Overall, 87 patients (35.2%) were upgraded, 20 (8.1%) were downgraded, and 140 (56.7%) had identical biopsy
and pathological Gleason sum groups. Smaller TRUS volume was significantly associated with increased likelihood of upgrading (p trend=0.022). Men with prostates 25 cm(3) or less had more than 2.7 times the risk of disease being upgraded relative to men with TRUS volumes more than 40 cm(3) (OR 2.718, 95% CI 1.403-8.126). Conclusion: In our study, smaller prostate volumes were at increased risk for GS upgrading after RP. This finding should be kept in mind when making treatment decisions for men with prostate cancer that appears to be of a low grade on biopsy, especially in Asian urologic fields.

[1199]
TÍTULO / TITLE: - Long Non-coding RNA GAS5 Functions as a Tumor Suppressor in Renal Cell Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Qiao HP; Gao WS; Huo JX; Yang ZS
INSTITUCIÓN / INSTITUTION: - School of Radiation Medicine and Protection, Medical College of Soochow University, Suzhou, Jiangsu, China E-mail : yangzhanshanyzs@hotmail.com.
RESUMEN / SUMMARY: - Background: Renal cell carcinoma (RCC) is a malignancy with a poor prognosis. We aimed to explore whether the expression of Long Non-Coding RNA (LncRNA) growth arrest-specific transcript 5 (GAS5) is associated with RCC genesis. Methods: We selected twelve clinical samples diagnosed for renal clear cell carcinoma and found that the LncRNA GAS5 transcript levels were significantly reduced relative to those in adjacent unaffected normal renal tissues. Results: In addition, expression of GAS5 was lower in the RCC cell line A498 than that in normal renal cell line HK-2. Furthermore, using functional expression cloning, we found that overexpression of GAS5 in A498 cells inhibited cell proliferation, induced cell apoptosis and arrested cell cycling. At the same time, the migration and invasion potential of A498 cells were inhibited compared to control groups. Conclusion: Our study provided the first evidence that a decrease in GAS5 expression is associated with RCC genesis and progression and overexpression of GAS5 can act as a tumor suppressor for RCC, providing a potential attractive therapeutic approach for this malignancy.

[1200]
TÍTULO / TITLE: - Gene expression is highly correlated on the chromosome level in urinary bladder cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Lambrou GI; Adamaki M; Delakas D; Spandidos DA; Vlahopoulous S; Zaravinos A
INSTITUCIÓN / INSTITUTION: First Department of Pediatrics; University of Athens; Choremeio Research Laboratory; Athens, Greece.

RESUMEN / SUMMARY: Objetivo: Mapas de correlaciones cromosómicas muestran correlaciones entre patrones de expresión genética en el mismo cromosoma. Nuestro objetivo fue mapear las genes en regiones cromosómicas y identificar correlaciones a través de su ubicación en regiones cromosómicas. Material y Métodos: Después de la análise de microarrays, utilizamos Ingenuity Pathway Analysis (IPA) para construir redes de genes de las moléculas co-dereguladas en cáncer de vejiga. Se realizaron mapeos cromosómicos, modelado matemático y simulaciones de datos utilizando los softwares WebGestalt y Matlab (®). Resultados: Las moléculas top co-dereguladas en 129 muestras de cáncer de vejiga implicaron las vías de señalización PI3K/AKT, cicle celular, Myc mediado apoptosis and ERK5 signaling pathways. Sus funciones moleculares y celulares más prominentes se relacionaron con ciclo celular, muerte celular, expresión genética, transporte molecular y crecimiento y proliferación celular. Los mapas de correlación cromosómica nos permitieron detectar genes expresados de manera similar a lo largo de los cromosomas. Identificamos fuertes correlaciones entre tumores de Talpha grado 1, así como para los de Talpha grado 2, en cromosomas 1, 2, 3, 7, 12 y 19. Domains de expresión genética se revelaron para los tejidos normales, así como. La expresión de los datos fueron simulados, exhibiendo un excelente fit (0.7 < R² < 0.9). Las simulaciones revelaron que a lo largo de los diferentes muestras, genes en los mismos cromosomas se expresan de manera similar. Conclusiones: La expresión genética está altamente correlacionada en el nivel cromosómico. Mapas de correlación cromosómica de perfiles de expresión genética pueden proporcionar más información sobre mecanismos de regulación genética. La expresión de datos genéticos se pueden simular usando funciones polinomiales.

TÍTULO / TITLE: Caracterización de SNPs asociados con cáncer de próstata en hombres de ascendencia ashkenazi desde el conjunto de GWAS identificados SNPs: impacto de historia familiar de cáncer y predicción SNP acumulativa.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Agalliu I; Wang Z; Wang T; Dunn A; Parikh H; Myers T; Burk RD; Amundadottir L
INSTITUCIÓN / INSTITUTION: - Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York, United States of America. ilir.agalliu@einstein.yu.edu

RESUMEN / SUMMARY: - BACKGROUND: Genome-wide association studies (GWAS) have identified multiple SNPs associated with prostate cancer (PrCa). Population isolates may have different sets of risk alleles for PrCa constituting unique population and individual risk profiles. METHODS: To test this hypothesis, associations between 31 GWAS SNPs of PrCa were examined among 979 PrCa cases and 1,251 controls of Ashkenazic descent using logistic regression. We also investigated risks by age at diagnosis, pathological features of PrCa, and family history of cancer. Moreover, we examined associations between cumulative number of risk alleles and PrCa and assessed the utility of risk alleles in PrCa risk prediction by comparing the area under the curve (AUC) for different logistic models. RESULTS: Of the 31 genotyped SNPs, 8 were associated with PrCa at p ≤ 0.002 (corrected p-value threshold) with odds ratios (ORs) ranging from 1.22 to 1.42 per risk allele. Four SNPs were associated with aggressive PrCa, while three other SNPs showed potential interactions for PrCa by family history of PrCa (rs8102476; 19q13), lung cancer (rs17021918; 4q22), and breast cancer (rs10896449; 11q13). Men in the highest vs. lowest quartile of cumulative number of risk alleles had ORs of 3.70 (95% CI 2.76-4.97); 3.76 (95% CI 2.57-5.50), and 5.20 (95% CI 2.94-9.19) for overall PrCa, aggressive cancer and younger age at diagnosis, respectively. The addition of cumulative risk alleles to the model containing age at diagnosis and family history of PrCa yielded a slightly higher AUC (0.69 vs. 0.64).

CONCLUSION: These data define a set of risk alleles associated with PrCa in men of Ashkenazic descent and indicate possible genetic differences for PrCa between populations of European and Ashkenazic ancestry. Use of genetic markers might provide an opportunity to identify men at highest risk for younger age of onset PrCa; however, their clinical utility in identifying men at highest risk for aggressive cancer remains limited.

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TÍTULO / TITLE: - Prostate Cancer Risk in Pre-Diabetic Men: A Matched Cohort Study.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Onitilo AA; Berg RL; Engel JM; Stankowski RV; Glurich I; Williams GM; Doi SA

INSTITUCIÓN / INSTITUTION: - *Department of Hematology/Oncology, Marshfield Clinic Weston Center, Weston, Wisconsin, USA.

RESUMEN / SUMMARY: - Background Diagnosis and duration of type 2 diabetes mellitus (DM) appears to be associated with decreased prostate cancer risk.
Limitations of previous studies include methods of subject selection and accurate definition of DM diagnosis. We examined the temporal relationship between DM and prostate cancer risk exploring the period of greatest risk starting from the prediabetic to the post-diabetic period using clinical and administrative data to accurately define the date of DM diagnosis. Methods We identified 5,813 men who developed DM between January 1, 1995 and December 31, 2009 (reference date, date of DM onset or matched date for non-diabetic cohort) and 28,019 non-diabetic men matched by age, smoking history, residence, and reference date. Prostate cancer incidence before and after the reference date was assessed using Cox regression modeling adjusted for matching variables, body mass index, insurance status, and comorbidities. Primary outcomes included hazard ratio (HR) and number needed to be exposed to DM for one additional person to be harmed (NNEH) or benefit (NNEB) with respect to prostate cancer risk. Results After full adjustment, the HR for prostate cancer before DM diagnosis was 0.96 (95% CI 0.85–1.08; P=0.4752), and the NNEB was 974 at DM diagnosis. After the reference date, the fully-adjusted HR for prostate cancer in diabetic men was 0.84 (95% CI 0.72–0.97, P=0.0167), and the NNEB 3 years after DM onset was 425. The NNEB continued to decrease over time, reaching 63 at 15 years after DM onset, suggesting an increasing protective effect of DM on prostate cancer risk over time. No significant difference between the diabetic and non-diabetic cohort was found prior to reference date. Conclusion Prostate cancer risk is not reduced in pre-diabetic men but decreases after DM diagnosis and the protective effect of DM onset on prostate cancer risk increases with DM duration.
metabonomics method in patients with stomach cancer could effectively detect distinct changes in urinary metabolites and had the capacity to detect cancer; therefore, it may be a valuable tool in earlier diagnosis. Furthermore, the detection and identification of altered metabolites in the current study may help elucidate possible mechanisms involved in stomach cancer.

[1204]

**TÍTULO / TITLE:** Comparative Effectiveness of Intensity-Modulated Radiotherapy and Conventional Conformal Radiotherapy in the Treatment of Prostate Cancer After Radical Prostatectomy.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** JAMA. Acceso gratuito al texto completo.

- Enlace a la Editora de la Revista http://jama.ama-assn.org/search.dtl
- Enlace al texto completo (gratuito o de pago) 1001/jamainternmed.2013.1020

**AUTORES / AUTHORS:** Goldin GH; Sheets NC; Meyer AM; Kuo TM; Wu Y; Sturmer T; Godley PA; Carpenter WR; Chen RC

**RESUMEN / SUMMARY:** IMPORTANCE Comparative effectiveness research of prostate cancer therapies is needed because of the development and rapid clinical adoption of newer and costlier treatments without proven clinical benefit. Radiotherapy is indicated after prostatectomy in select patients who have adverse pathologic features and in those with recurrent disease. OBJECTIVES To examine the patterns of use of intensity-modulated radiotherapy (IMRT), a newer, more expensive technology that may reduce radiation dose to adjacent organs compared with the older conformal radiotherapy (CRT) in the postprostatectomy setting, and to compare disease control and morbidity outcomes of these treatments. DESIGN AND SETTING Data from the Surveillance, Epidemiology, and End Results-Medicare-linked database were used to identify patients with a diagnosis of prostate cancer who had received radiotherapy within 3 years after prostatectomy. PARTICIPANTS Patients who received IMRT or CRT. MAIN OUTCOMES AND MEASURES The outcomes of 457 IMRT and 557 CRT patients who received radiotherapy between 2002 and 2007 were compared using their claims through 2009. We used propensity score methods to balance baseline characteristics and estimate adjusted incidence rate ratios (RRs) and their 95% CIs for measured outcomes. RESULTS Use of IMRT increased from zero in 2000 to 82.1% in 2009. Men who received IMRT vs CRT showed no significant difference in rates of long-term gastrointestinal morbidity (RR, 0.95; 95% CI, 0.66-1.37), urinary nonincontinent morbidity (0.93; 0.66-1.33), urinary incontinence (0.98; 0.71-1.35), or erectile dysfunction (0.85; 0.61-1.19). There was no significant
difference in subsequent treatment for recurrent disease (RR, 1.31; 95% CI, 0.90-1.92). CONCLUSIONS AND RELEVANCE Postprostatectomy IMRT and CRT achieved similar morbidity and cancer control outcomes. The potential clinical benefit of IMRT in this setting is unclear. Given that IMRT is more expensive, its use for postprostatectomy radiotherapy may not be cost-effective compared with CRT, although formal analysis is needed.

[1205]
TÍTULO / TITLE: - Treating small renal masses: Costing it out.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 5489/cuaj.718
AUTORES / AUTHORS: - Yap SA; Finelli A; Alibhai SM
INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Surgery, University of Toronto, Toronto, ON;

[1206]
TÍTULO / TITLE: - Bladder cancer: Outpatient laser ablation is an option for localized bladder cancer treatment.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.120
AUTORES / AUTHORS: - Fenner A

[1207]
TÍTULO / TITLE: - Indole-3-Carbinol and 3',3'-Diindolylmethane Modulate Androgen’s Effect on C-C Chemokine Ligand 2 and Monocyte Attraction to Prostate Cancer Cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1158/1940-6207.CAPR-12-0419
AUTORES / AUTHORS: - Kim EK; Kim YS; Milner JA; Wang TT
INSTITUCIÓN / INSTITUTION: - U.S. Department of Agriculture, Building 307C, Room 132, BARC-EAST, 10300 Baltimore Ave., Beltsville, MD 20705. tom.wang@ars.usda.gov.
RESUMEN / SUMMARY: - Inflammation has a role in prostate tumorigenesis. Recruitment of inflammatory monocytes to the tumor site is mediated by C-C chemokine ligand 2 (CCL2) through binding to its receptor CCR2. We hypothesized that androgen could modulate CCL2 expression in hormone-
responsive prostate cancer cells and thereby promote recruitment of monocytes. Given the inhibitory effect of broccoli-derived compounds indole-3-carbinol (I3C) and 3,3'-diindolylmethane (DIM) on androgen-dependent pathways, we also reasoned that I3C and DIM could modulate the effect of androgen on CCL2-mediated pathways. Dihydrotestosterone was found to induce a time-dependent (0-72 hours) and concentration-dependent (0-1 nmol/L) increase in CCL2 mRNA levels in androgen-responsive human prostate cancer cells (LNCaP). This increase in CCL2 mRNA corresponded with increased secretion of CCL2 protein. The effect of dihydrotestosterone was mediated through an androgen receptor (AR)-dependent pathway as small inhibitor RNA against AR negated the induction of CCL2. Although dihydrotestosterone also induced TWIST1 mRNA, an epithelial-mesenchymal transition-related factor, and purported inducer of CCL2, blocking its expression with small inhibitor RNA did not inhibit dihydrotestosterone induction of CCL2 mRNA. Moreover, conditioned media from androgen-treated cells promoted human monocyte THP-1 cell migration and this effect was blocked by antibody against CCL-2. Both I3C and DIM inhibited promotional effects of dihydrotestosterone on CCL2 and migration. These results show that androgen may regulate CCL2 and promote inflammatory microenvironment in prostate tumors and that this process can be blocked by broccoli-derived compounds.

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[1208]
TÍTULO / TITLE: - Loss of SUMOylation on ATF3 Inhibits Proliferation of Prostate Cancer Cells by Modulating CCND1/2 Activity.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Wang CM; Yang WH
INSTITUCIÓN / INSTITUTION: - Department of Biomedical Sciences, Mercer University School of Medicine, Savannah, GA 31404, USA.
yang_w@mercer.edu.
RESUMEN / SUMMARY: - SUMOylation plays an important role in regulating a wide range of cellular processes. Previously, we showed that ATF3, a stress response mediator, can be SUMOylated and lysine 42 is the major SUMO site. However, the significance of ATF3 SUMOylation in biological processes is still poorly understood. In the present study, we investigated the role of ATF3 SUMOylation on CCND activity and cellular proliferation in human prostate cancer cells. First, we showed that ATF3 can be SUMOylated endogenously in the overexpression system, and lysine 42 is the major SUMO site. Unlike normal prostate tissue and androgen-responsive LNCaP cancer cells, androgen-independent PC3 and DU145 cancer cells did not express ATF3
endogenously. Overexpression of ATF3 increased CCND1/2 expression in PC3 and DU145 cancer cells. Interestingly, we observed that SUMOylation is essential for ATF3-mediated CCND1/2 activation. Finally, we observed that SUMOylation plays a functional role in ATF3-mediated cellular proliferation in PC3 and DU145 cells. Taken together, our results demonstrate that SUMO modification of ATF3 influences CCND1/2 activity and cellular proliferation of prostate cancer PC3 and DU145 cells and explains at least in part how ATF3 functions to regulate cancer development.

[1209]
TITULO / TITLE: - Evaluation of a bladder cancer cluster in a population of criminal investigators with the bureau of alcohol, tobacco, firearms and explosives-part 2: the association of cancer risk and fire scene investigation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Davis SR; Tao X; Bernacki EJ; Alfriend AS; Delowery ME
INSTITUCIÓN / INSTITUTION: - Federal Occupational Health, United States Department of Health and Human Services, 4550 Montgomery Avenue, Suite 950, Bethesda, MD 20814, USA.
RESUMEN / SUMMARY: - This study evaluated the association of bladder cancer risk and fire scene investigation within a cohort of white male criminal investigators with the United States Bureau of Alcohol, Tobacco, Firearms and Explosives that was found to be at increased risk for bladder cancer. Medical surveillance data were used in a nested case-control study to determine odds ratios (ORs) estimating the relative risk of the cancer associated with post-fire investigation. The study comprised seven bladder cancer cases and 1525 controls. Six of the cases reported holding assignments associated with post-fire investigation. The OR for bladder cancer was 19.01 (95% confidence interval = 1.94-186.39) for those holding any one or more of these assignments for one to four years versus zero years and 12.56 (1.14-138.58) for those holding any one or more of these assignments for five or more years versus zero years. The risk for bladder cancer is significantly elevated for those holding post-fire investigation assignments compared to those not holding these assignments.

[1210]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
A recent prostate cancer (PCa) genome-wide association study (GWAS) identified rs103294, a single nucleotide polymorphism (SNP) located on LILRA3, a key component in the regulation of inflammatory inhibition, to be significantly associated with PCa risk in a Chinese population. Because inflammation may be a common etiological risk factor between PCa and benign prostatic hyperplasia (BPH), the current study was conducted to investigate the association of rs103294 with BPH risk. rs103294 was genotyped in a Chinese population of 426 BPH cases and 1,008 controls from Xinhua Hospital in Shanghai, China. Association between rs103294, BPH risk and clinicopathological traits were tested with adjustment for age. rs103294 was significantly associated with BPH risk with a p-value of 0.0067. Individuals with risk allele “C” had increased risk for BPH (OR = 1.34, 95% CI: 1.09-1.66). Stratified analysis revealed a stronger association risk for younger patients who are below 72 years old (OR = 1.51, 95% CI: 1.06-2.16). Our study represents the first effort to demonstrate that LILRA3 gene is significantly associated with BPH risk in a Chinese population. Our results support a common role of inflammation in the development of PCa and BPH. Additional studies are needed to further evaluate our results.
therapy undergoing PVP, and compared the results with patients who did not take anticoagulation therapy. A total of 89 patients who received photoselective vaporization laser for benign prostate hyperplasia from May 2006 to February 2011 in our hospital were enrolled in our study. The patients were divided into two groups based on whether or not they were taking oral aspirin; 23 (25.8%) patients were taking aspirin derivatives (aspirin group), and 66 (74.2%) were not taking aspirin derivatives (control group). The mean prostate volume (58.8 mL vs 51 mL; $P = 0.16$) and mean energy consumption (235,268 J vs 289,793 J; $P = 0.097$) were comparable between the aspirin group and control group. The average postoperative results of hemoglobin were 13.4 mg/dL for the aspirin group versus 13.9 mg/dL for the control group ($P = 0.327$). A significantly higher maximum flow rates and 80% improved post-void residual urine were noted during the followup. Postoperatively all variable showed significant improvement starting at month 1 of followup and remained improved for the 12 month followup. Postoperative complications were low and comparable between groups. PVP was characterized by excellent hemostatic properties and a very low intraoperative complication rate, even in the patients who were taking aspirin. On the basis of our perioperative results, we recommend PVP as a safe and effective procedure for patients with symptomatic benign prostate hyperplasia when taking an aspirin derivative.

[1212] TÍTULO / TITLE: - Inhibition of CCL2 Signaling in Combination with Docetaxel Treatment Has Profound Inhibitory Effects on Prostate Cancer Growth in Bone.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kirk PS; Koreckij T; Nguyen HM; Brown LG; Snyder LA; Vessella RL; Corey E
INSTITUCIÓN / INSTITUTION: - Department of Urology, University of Washington, Seattle, WA 98195, USA. ecorey@uw.edu.
RESUMEN / SUMMARY: - The C-C chemokine ligand 2 (CCL2) stimulates migration, proliferation, and invasion of prostate cancer (PCa) cells, and its signaling also plays a role in the activation of osteoclasts. Therefore targeting CCL2 signaling in regulation of tumor progression in bone metastases is an area of intense research. The objective of our study was to investigate the efficacy of CCL2 blockade by neutralizing antibodies to inhibit the growth of PCa in bone. We used a preclinical model of cancer growth in the bone in which PCa C4-2B cells were injected directly into murine tibiae. Animals were treated for ten weeks with neutralizing anti-CCL2 antibodies, docetaxel, or a combination of both, and then followed an additional nine weeks. CCL2 blockade inhibited the growth of PCa in bone, with even more pronounced
inhibition in combination with docetaxel. CCL2 blockade also resulted in increases in bone mineral density. Furthermore, our results showed that the tumor inhibition lasted even after discontinuation of the treatment. Our data provide compelling evidence that CCL2 blockade slows PCa growth in bone, both alone and in combination with docetaxel. These results support the continued investigations of CCL2 blockade as a treatment for advanced metastatic PCa.

[1213]
TÍTULO / TITLE: - Portal Hypertension in Childhood Bilateral Wilms’ Tumor Survivor: An Excellent Indication for TIPS.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Nakib G; Calcaterra V; Brunero M; Goruppi I; Quaretti P; Moramarco LP; Bruno R; Raffaele A; Pelizzo G
INSTITUCIÓN / INSTITUTION: - Department of the Mother and Child Health, Pediatric Surgery Unit, IRCCS Policlinico San Matteo Foundation and University of Pavia, Piazzale Golgi 2, 27100 Pavia, Italy.
RESUMEN / SUMMARY: - Introduction. Increased pressure in portal venous system is relatively a rare complication after chemoradiotherapy for Wilms’ tumor (WT). In paediatric population, feasibility and efficacy of transjugular intrahepatic portosystemic shunt (TIPS) in portal hypertension nonresponsive to medical or endoscopic treatment have been recently advocated. We report a case of TIPS positioning in a 15-year-old girl with portal hypertension as a long-term sequel of multimodality therapy in bilateral WT. Case Report. Two-year-old girl was diagnosed for bilateral WT. Right nephrectomy with left heminephrectomy and chemoradiotherapy were performed. At 7 years of age, the first gastrointestinal bleeding appeared, followed by another episode two years later, both were treated successfully with beta-blockers. At 15 years of age, severe unresponsive life-threatening gastrointestinal bleeding without hepatosplenomegaly was managed by TIPS. Reduction of the portosystemic pressure gradient was obtained. Conclusion. TIPS positioning for portal hypertension in long-term tumors’ sequel is feasible and could be considered as an additional indication in paediatric patients.

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[1214]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
BACKGROUND: Docetaxel is an established first-line therapy to treat metastatic castration-resistant prostate cancer (mCRPC). Recently, abiraterone and cabazitaxel were approved for use after docetaxel failure, with improved survival. National Institute for Health and Clinical Excellence (NICE) preliminary recommendations were negative for both abiraterone (now positive in final recommendation) and cabazitaxel (negative in final recommendation). OBJECTIVE: To evaluate the cost-effectiveness of abiraterone, cabazitaxel, mitoxantrone and prednisone for mCRPC treatment in US. METHODS: A decision-tree model was constructed to compare the two mCRPC treatments versus two placebos over 18 months from a societal perspective. Chance nodes include baseline pain as a severity indicator, grade III/IV side-effects, and survival at 18 months. Probabilities, survival and health utilities were from published studies. Model cost inputs included drug treatment, side-effect management and prevention, radiation for pain, and death associated costs in 2010 US dollars. RESULTS: Abiraterone is a cost-effective choice at $94K/QALY (quality adjusted life years) compared to placebo in our base-case analysis. Cabazitaxel and abiraterone are the most effective, yet also most expensive agents. The incremental cost-effectiveness ratios (ICER) at base-case are $101K/QALY (extended dominated) for mitoxantrone vs. placebo, $91K/QALY for abiraterone vs. mitoxantrone, $956K/QALY for cabazitaxel vs. abiraterone. Abiraterone becomes less cost-effective as its AWP increases, or if the cost of mitoxantrone side-effect management decreases. Increases in the percentage of patients with baseline pain leads to an increased ICER for both mitoxantrone and abiraterone, but mitoxantrone does relatively better. Cabazitaxel remains not cost-effective. CONCLUSION: Our base case model suggests that abiraterone is a cost-effective option in docetaxel-refractory mCRPC patients. Newer treatments will also need a CEA assessment compared to abiraterone.

[1215]

TÍTULO / TITLE: - Advances in the design and discovery of drugs for the treatment of prostatic hyperplasia.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Kumar R; Malla P; Kumar M
INTRODUCTION: Benign prostatic hyperplasia (BPH) is a common medical problem in nearly 80% of geriatric male population severely affecting the quality of life. Several strategies have been suggested in the past for the management of BPH, but only alpha-blockers and 5alpha-reductase inhibitors are in clinical use. This review aims to give deep insight into advances in the design and discovery of newer chemical entities as ‘druggable’ molecule for the management of BPH. Areas covered: In this review, the authors cover various classes of drugs that have shown their potential for management of BPH. These drugs include alpha-adrenergic antagonists, 5alpha-reductase inhibitors, phytochemical agents, phosphodiesterase inhibitor, luteinizing hormone releasing hormone antagonists and muscarinic receptor antagonists. Literature searches were carried out using Google Scholar, SciFinder and PubMed. Expert opinion: The exact etiology of BPH is unknown; however, several mechanisms may be involved in the progression of the disease. Beside surgery and watchful waiting, medical therapies to treat BPH include alpha-adrenergic antagonist and 5alpha-reductase inhibitors. Phytotherapeutic agents are also used in some countries. Various other chemical classes of drugs are proposed for the treatment of the disease, but none of them have reached the clinic. Many classes of drugs are currently undergoing clinical trials such as phosphodiesterase inhibitors, luteinizing hormone releasing hormone antagonists and muscarinic receptor antagonists. The current need is to develop a potent, efficacious and highly selective drug for the treatment of BPH.

TÍTULO / TITLE: Correlation of tumor relapse and elevated expression of survivin and vascular endothelial growth factor in superficial bladder transitional cell carcinoma.

RESUMEN / SUMMARY: Survivin and vascular endothelial growth factor (VEGF) are newly discovered tumor markers closely correlated with bladder cancer. We analyzed the expression of survivin and VEGF in paraffin-embedded tumor tissues from 78 patients with bladder transitional cell carcinoma (BTCC) using an immunohistochemistry method. Normal bladder mucosae from 10 non-

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INSTITUCIÓN / INSTITUTION: Department of Urology, Second Hospital of Shandong University, Jinan, China.
BTCC cases were also included as a control group. All patients were closely followed up for tumor recurrence after undergoing transurethral resection of bladder tumor procedures. The positive expression rates of survivin and VEGF in superficial BTCC were 66.7% (52/78) and 69.2% (54/78), respectively, which were significantly higher than those in the control group, 0% (0/10). A positive correlation was found between survivin and VEGF expression (r = 0.283, P < 0.01). Thirty-two of 78 patients (41.0%) displayed recurrence during follow-up (median: 47; range: 7-62 months). The tumor recurrence rate in survivin(+) patients was 53.8% (28/52), which was significantly higher than that in survivin (-) patients [15.4% (4/26); P < 0.05]. The recurrence rate in VEGF(+) / VEGF(-) patients was 50.0% (27/54) and 20.8% (5/24), respectively (P < 0.05). The sensitivity for predicting the relapse of superficial BTCC was 87.5% in the survivin(+) group, 84.4% in the VEGF(+) group, and 78.1% in the survivin(+)/VEGF(+) group, and the specificity was 47.8, 41.3, and 65.2%, respectively. Survivin and VEGF interact and jointly regulate the biological behavior of bladder cancer. Our results suggest that overexpression of survivin and VEGF accompany a higher risk of BTCC recurrence, making survivin and VEGF biomarkers for predicting the relapse of bladder cancer.
significantly (P<0.05). Of the 11 patients, 7 patients required one treatment, 4 patients two treatment, and 1 patients three treatment. 2 patients who had a documented urinary incontinence prior to the laser treatment subsequently required artificial urinary sphincter implantation and reported satisfaction without developing any recurrent strictures or artificial urinary sphincter erosion. All patients exhibited well-healed strictures and could void without difficulty.

CONCLUSIONS: HOLMIUM: YAG laser therapy represents a safe, effective and minimally invasive treatment for urethral/bladder neck strictures occurring secondary to high-intensity focused ultrasound for prostate cancer.

[1218]

TÍTULO / TITLE: - A novel IgE antibody targeting the prostate-specific antigen as a potential prostate cancer therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Daniels-Wells TR; Helguera G; Leuchter RK; Quintero R; Kozman M; Rodriguez JA; Ortiz-Sanchez E; Martinez-Maza O; Schultes BC; Nicodemus CF; Penichet ML
INSTITUCIÓN / INSTITUTION: - Division of Surgical Oncology, Department of Surgery, David Geffen School of Medicine, University of California, Los Angeles, CA, USA. tdaniels@mednet.ucla.edu.

RESUMEN / SUMMARY: - BACKGROUND: Prostate cancer (PCa) is the second leading cause of cancer deaths in men in the United States. The prostate-specific antigen (PSA), often found at high levels in the serum of PCa patients, has been used as a marker for PCa detection and as a target of immunotherapy. The murine IgG1 monoclonal antibody AR47.47, specific for human PSA, has been shown to enhance antigen presentation by human dendritic cells and induce both CD4 and CD8 T-cell activation when complexed with PSA. In this study, we explored the properties of a novel mouse/human chimeric anti-PSA IgE containing the variable regions of AR47.47 as a potential therapy for PCa. Our goal was to take advantage of the unique properties of IgE in order to trigger immune activation against PCa. METHODS: Binding characteristics of the antibody were determined by ELISA and flow cytometry. In vitro degranulation was determined by the release of beta-hexosaminidase from effector cells. In vivo degranulation was monitored in human FcepsilonRIalpha transgenic mice using the passive cutaneous anaphylaxis assay. These mice were also used for a vaccination study to determine the in vivo anti-cancer effects of this antibody. Significant differences in survival were determined using the Log Rank test. In vitro T-cell activation was studied using human dendritic cells and autologous T cells. RESULTS: The anti-PSA IgE, expressed in murine myeloma cells, is properly assembled and secreted, and binds the antigen and
FcepsilonRI. In addition, this antibody is capable of triggering effector cell degranulation in vitro and in vivo when artificially cross-linked, but not in the presence of the natural soluble antigen, suggesting that such an interaction will not trigger systemic anaphylaxis. Importantly, the anti-PSA IgE combined with PSA also triggers immune activation in vitro and in vivo and significantly prolongs the survival of human FcepsilonRIalpha transgenic mice challenged with PSA-expressing tumors in a prophylactic vaccination setting.

CONCLUSIONS: The anti-PSA IgE exhibits the expected biological properties and is capable of triggering immune activation and anti-tumor protection. Further studies on this antibody as a potential PCa therapy are warranted.

[1219]
TÍTULO / TITLE: - Isolation and culture of human spermatogonial stem cells derived from testis biopsy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Goharbakhsh L; Mohazzab A; Salehkhou S; Heidari M; Zarnani AH; Parivar K; Akhondi MM
INSTITUCIÓN / INSTITUTION: - Department of Biology, Faculty of Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran ; Reproductive Biotechnology Research Center, Avicenna Research Institute, ACECR, Tehran, Iran.
RESUMEN / SUMMARY: - BACKGROUND: In cancer patients, chemo and radiotherapy can cause infertility by damaging spermatogenesis process. This process is based on self-renewal and differentiation of a rare population of the testicular cells called Spermatogonial Stem Cells (SSCs). Scientists have tried to isolate, enrich and culture Human spermatogonial stem cells, hoping to resolve infertility problems in cancer recovered patients in the future.
METHODS: Spermatogonial stem cells were isolated and purified from human testicular biopsies sample consisting of at least 500,000 and at most 2,000,000 cells. Two enzymatic digestion steps were performed. Enriching methods, differential plating, and specific culture in serum-free medium with added growth factors: human GDNF, bFGF, EGF and LIF was performed on coated dishes.
RESULTS: Human spermatogonial stem cell clusters were observed after 7 to 10 days in specific culture, then after several passages and successful expanding duration of 52 days, the cells were evaluated by three layer immunocytochemistry test (LSAB) to stain GPR125 protein as a surface marker in human spermatogonial stem cells. CONCLUSION: In current study human spermatogonial stem cell were isolated and expanded with the least manipulations in comparison with the other usual isolation methods like florescent or magnetic activated cell sorting. In contrast to the other SSCs isolation and culture methods, this system is based on the testicular biopsies
against large samples, thus suggested method in this study is closer to clinical usage in the future.

[1220]

TÍTULO / TITLE: - The Establishment of K-CaP (the Multicenter Korean Prostate Cancer Database).

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Lee DH; Lee SH; Rha KH; Choi IY; Lee JY; Kim SW; Lee S; Hong SK; Byun SS; Jeong IG; Hong JH; Kim CS; Jeon HG; Lee HM; Chung BH

INSTITUCIÓN / INSTITUTION: - Department of Urology, Urological Science Institute, Yonsei University College of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - PURPOSE: The purpose of this article was to announce the establishment of the multicenter Korean Prostate Cancer Database (K-CaP) and to provide urologists with details about K-CaP’s methodology.

MATERIALS AND METHODS: The initial participating K-CaP institutions include five medical centers in Korea. First, we registered prostate cancer patients who underwent radical prostatectomy as the basic background data. K-CaP is poised to combine these initial observational longitudinal studies with those of other eligible institutions as the database grows. All current prostate cancer patients in Korea are able to be registered into the Web-based database system and thereby have a role in several observational studies. The structure of the database for K-CaP was developed by matching it with the respective data from different studies. The operability of the K-CaP database system was verified by using the existing databases from three participating institutions.

RESULTS: The analysis of clinicopathologic characteristics of patients with the use of the Web-based database was successfully conducted. We confirmed the accurate operation of the Web-based database system without any difficulties.

CONCLUSIONS: We are announcing the establishment of K-CaP the first database of comprehensive observational longitudinal studies about prostate cancer in Korea. The database will be successfully maintained by sufficiently and continuously updating all patient data covering several treatments. Complete statistical results for registered prostate cancer patients are forthcoming for the basic background data to establish the database. Even though much trial and error are expected during the development process, we expect that K-CaP will eventually become one of the most powerful longitudinal observation databases.

[1221]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Viani GA; da Silva LB; da Silva BB; Crempe YB; Martins VS; Ferrari RJ; Polo MC; Rossi BT; Suguikawa E; Zulliani GC; Stefano EJ

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Marilia Medical School, Marilia, Sao Paulo, Brazil. gusviani@gmail.com.

RESUMEN / SUMMARY: - PURPOSE: To compare the acute toxicities in radical treatment of prostate cancer between conventional schedule (C-ARM) with 78 Gy/39 fractions and hypofractionation conformal treatment (H-ARM) with 69 Gy/23 fractions. METHODS AND MATERIAL: This prospective double arm study consisted of 217 patients with prostate cancer, 112 in H-ARM and 105 in C-ARM arm. C-ARM received conventional six-field conformal radiotherapy with 78 Gy in 39 fractions while H-ARM received hypofractionation with 69 Gy in 23 fractions. Weekly assessment of acute reactions was done during treatment and with one, and 3 months using RTOG scale. Univariated analysis was performed to evaluate differences between the incidences of acute reaction in the treatment arms. Variables with p value less than 0.1 were included in the multivariated logistic regression. RESULTS: There was no difference between H-ARM versus C-ARM for severity and incidence in genitourinary (GU) and gastrointestinal (GI) acute toxicity. During the treatment comparing H-ARM with C-ARM no differences was observed for GI toxicity (grade 0-3; H-ARM = 45.5%, 34%, 18.7% and 1.8% versus C-ARM = 47.6%, 35.2%, 17.2% and 0). For acute GU toxicity no difference was detected between H-ARM (grade 0-3; 22.3%, 54.5%, 18.7% and 4.5%) and C-ARM (grade 0-3; 25.8%, 53.3%, 17.1% and 3.8%). At the 3-months follow-up, persistent Grade > =2 acute GU and GI toxicity were 2.5% and 1.8% in H-ARM versus 5.7% and 3% in C-ARM (p > 0.05). In univariated and multivariated analyses, there was not any dosimetric predictor for GI and GU toxicity. CONCLUSIONS: Our data demonstrate that hypofractionated radiotherapy achieving high biological effective dose using conformal radiotherapy is feasible for prostate cancer, being well tolerated with minimal severe acute toxicity.

[1222]

TÍTULO / TITLE: - Mixed epithelial and stromal tumor of the kidney.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Zheng S; Yuan HC; Liu LR; Wei Q; Han P

893
INSTITUCIÓN / INSTITUTION: - Department of Urology, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

RESUMEN / SUMMARY: - A 44-year-old woman who underwent radical nephrectomy due to a left renal mass presented to our clinic. Results of the histopathological examination showed a mixed epithelial and stromal tumor of the kidney, a rare benign lesion of the kidney. The epidemiology, histopathological features, imaging features, possible pathogeneses, and treatment alternatives are discussed, and the relevant literature is reviewed. The postoperative course was uneventful, and the patient was free of local recurrence or metastasis until the last follow-up (12 months).

[1223]

TÍTULO / TITLE: - Modelling synergistic interactions between HER2, Sprouty2 and PTEN in driving prostate carcinogenesis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ahmad I; Gao M; Patel R; Leung HY

[1224]

TÍTULO / TITLE: - Application of the revised Tumour Node Metastasis (TNM) staging system of clear cell renal cell carcinoma in eastern China: advantages and limitations.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Qin C; Sun LJ; Cui L; Cao Q; Zhu J; Li P; Zhang GM; Mao X; Shao PF; Wang ML; Zhang ZD; Gu M; Zhang W; Yin CJ
INSTITUCIÓN / INSTITUTION: - Department of Urology, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China.
RESUMEN / SUMMARY: - This study was designed to evaluate whether the revised 2010 Tumour Node Metastasis (TNM) staging system could lead to a more accurate prediction of the prognosis of renal cell carcinoma (RCC) patients. A total of 1216 patients who had undergone radical nephrectomy or partial nephrectomy for RCC from 2003 to 2011 were enrolled. All of the patients had pathologically confirmed clear cell RCC (ccRCC). All cases were
staged by both the 2002 and 2010 TNM staging systems after pathological review, and survival data were collected. Univariate and multivariate Cox regression models were used to evaluate cancer-specific survival (CSS) and progression-free survival (PFS) after surgery. Continuous variables, such as age and tumour diameter, were calculated as mean values and standard deviations (s.d.) or as median values. Survival was calculated by the Kaplan-Meier method, and the log-rank test assessed differences between groups. Statistically significant differences in CSS and PFS were noted among patients in T3 subgroups using the new 2010 staging system. Therefore, the revised 2010 TNM staging system can lead to a more accurate prediction of the prognosis of ccRCC patients. However, when using the revised 2010 staging system, we found that more than 92% of patients (288/313) with T3 tumours were staged in the T3a subgroup, and their survival data were not significantly different from those of patients with T2b tumours. In addition, T2 subclassification failed to independently predict survival in RCC patients.

[1225]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Demirci U; Canda AE; Dede DS; Cakici OU; Akinci MB; Yalcin B
INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Ataturk Training and Research Hospital, Ankara, Turkey E-mail: drumutedemirci@gmail.com.
RESUMEN / SUMMARY: - Background: Upper tract transitional cell carcinomas (UTCC) are relatively uncommon but prognosis is generally worse than TCC of bladder. Methods: Between March 2004 and June 2012, patients with initial non-metastatic UTCC were assessed in the Medical Oncology and Urology Departments of Ataturk Training and Research Hospital. Results: A total of 11 patients with initially non-metastatic UTCC were detected in the 8 year period, all males. Median age of was 62 (range, 38-74). Six lesions were located in the renal pelvis and 5 in the ureter. Nephroureterectomy was performed in 9 patients, and distal ureterectomy and cuff excision of the bladder in the remaining 2. The majority (n= 9) had high grade tumors. Median primary tumor diameter was 3.5 cm (range, 0.7-10). Five patients (45.5%) were stage I, 2 (18.2%) were stage II, and 4 (36.4%) were stage III. While adjuvant chemotherapy was not applied for stage I and II disease (n= 7), 4 to 6 courses were applied for 3 of the stage III patients. Also one stage III case received adjuvant radiotherapy. Up to 100 months follow-up, median overall survival was
13 months (range, 5-100 months). While stage I and II patients are following-up without muscle-invasive progression, 2 of stage III patients demonstrated progression. Conclusion: We need more collaborative studies to determine management of especially pT3-pT4 patients with UTCC.

[1226]
TÍTULO / TITLE: - Prostate cancer research in China.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Ren SC; Chen R; Sun YH

[1227]
TÍTULO / TITLE: - A tight junction between E-Cadherin and the prostate tumor suppressor SPDEF.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Coppola V; Bonci D

[1228]
TÍTULO / TITLE: - Benign prostate hyperplasia: average volume in southwestern Nigerians and correlation with anthropometrics.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Badmus TA; Asaley CM; Badmus SA; Takure AO; Ibrahim MH; Arowolo OA
OBJECTIVES: To determine the prevalent age of symptomatic benign prostate hyperplasia (BPH), the average BPH volume, and the association between BPH volumes and the age, and anthropometrics in our immediate black community. PATIENTS, MATERIALS AND METHOD: Selected patients with lower urinary tract symptoms (LUTS) due to BPH with tissue diagnosis, and adult men of similar age group with no irritative or obstructive LUTS were prospectively studied from July 2003 to June 2009. The age, height and weight were recorded, prostate volumes determined with ultrasound, body mass index (bmi) calculated, and correlations determined between the prostate volume and the age, and anthropometrics. RESULTS: 105 patients aged 43-88yrs (mean=64.4, 8.88SD) managed for BPH were studied with 93 asymptomatic men aged 43-80yrs (mean=56.15, 9.89SD). The mean(SD) prostate volume, height, weight and bmi were 83.8(37.7)ml, 1.67(0.07)m, 63.6(9.32)kg and 22.8(3.03)kg/m2, and 24.5(9.2)ml, 1.69(0.06)m, 68.9(10.6)kg and 24.2(3.44)kg/m2 respectively for symptomatic and asymptomatic groups. In the symptomatic group, BPH volume showed significant positive correlation with the age (p=0.030), but no correlation with the weight (p=0.550), height (p=0.375) and bmi (p=0.840). In the asymptomatic group, prostate volume also showed significant positive correlation with the age (p=0.041), but no correlation with the weight (p=0.434), height (p=0.394), and bmi (p=0.203). Conclusion: The prevalent age of symptomatic BPH in our community is 43-88years with 83.79(37.66)ml mean(SD) volume in symptomatic patients and 24.45(9.21)ml in asymptomatic men. BPH volume correlates with age but not with anthropometrics. Lack of correlation with BPH volume suggests that anthropometrics may not be risk factors for development of BPH in our community.
human carcinoma cells. While MMPs are thought to regulate the dynamics of extracellular matrix turnover, new evidence shows that these enzymes may play a critical regulatory role in inflammation. To investigate the role of MMP-26 in inflammation, three different variants of androgen repressed human prostate cancer (ARCaP) cells were investigated in the study: parental, MMP-26 sense cDNA-transfected, and MMP-26 antisense cDNA-transfected ARCaP cells. Protein lysates and RNA from control and genetically modified cells were analyzed by Western blotting and real-time reverse transcription polymerase chain reaction on arrays of genes critical to the inflammatory response. In comparison to parental controls, up-regulation of MMP-26 expression in MMP-26 sense cDNA-transfected cells resulted in a decrease in inflammatory genes expression. Conversely, inflammatory genes were up-regulated in MMP-26 antisense cDNA-transfected cells. Therefore, modulation of MMP-26 levels significantly affects the expression of inflammatory genes, suggesting an anti-inflammatory role of MMP-26. To determine a possible mechanism of action, further analysis, at both transcript and protein levels, revealed a dramatic down-regulation of interleukin-10 receptor B (IL10RB) in MMP-26 antisense cDNA-transfected cells. The low level of IL10RB was inversely correlated with matrix metalloproteinase-9 (MMP-9) expression. Collectively, our data suggest that the deficiency of MMP-26 may promote inflammation via inhibition of IL10RB-mediated signaling. These results propose a novel anti-inflammation function of MMP-26 and could provide novel molecular insight of therapeutic targeting.

[1230]

**TÍTULO / TITLE:** - Propagation of Human Prostate Cancer Stem-Like Cells Occurs through EGFR-Mediated ERK Activation.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago)

**AUTORES / AUTHORS:** - Rybak AP; Ingram AJ; Tang D

**INSTITUCIÓN / INSTITUTION:** - Division of Nephrology, Department of Medicine, McMaster University, Hamilton, Ontario, Canada ; Father Sean O'Sullivan Research Institute, Hamilton, Ontario, Canada ; The Hamilton Centre for Kidney Research (HCKR), St. Joseph’s Hospital, Hamilton, Ontario, Canada.

**RESUMEN / SUMMARY:** - Prostate cancer stem-like cells (PCSCs) are being intensely investigated largely owing to their contributions towards prostate tumorigenesis, however, our understanding of PCSC biology, including their critical pathways, remains incompletely understood. While epidermal growth factor (EGF) is widely used in maintaining PCSC cells in vitro, the importance of EGF-dependent signaling and its downstream pathways in PCSC self-renewal are not well characterized. By investigating DU145 sphere cells, a population of
prostate cancer cells with stem-like properties, we report here that epidermal growth factor receptor (EGFR) signaling plays a critical role in the propagation of DU145 PCSCs. Activation of EGFR signaling via addition of EGF and ectopic expression of a constitutively-active EGFR mutant (EGFRvIII) increased sphere formation. Conversely, inhibition of EGFR signaling by using EGFR inhibitors (AG1478 and PD168393) and knockdown of EGFR significantly inhibited PCSC self-renewal. Consistent with the MEK-ERK pathway being a major target of EGFR signaling, activation of the MEK-ERK pathway contributed to EGFR-facilitated PCSC propagation. Modulation of EGFR signaling affected extracellular signal-related kinase (ERK) activation. Inhibition of ERK activation through multiple approaches, including treatment with the MEK inhibitor U0126, ectopic expression of dominant-negative MEK1(K97M), and knockdown of either ERK1 or ERK2 resulted in a robust reduction in PCSC propagation. Collectively, the present study provides evidence that EGFR signaling promotes PCSC self-renewal, in part, by activating the MEK-ERK pathway.

[1231]

TÍTULO / TITLE: PTPL1 and PKCdelta contribute to proapoptotic signalling in prostate cancer cells.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Castilla C; Chinchon D; Medina R; Torrubia FJ; Japon MA; Saez C
INSTITUCIÓN / INSTITUTION: Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocio/CSIC/Universidad de Sevilla, Seville 41013, España.
RESUMEN / SUMMARY: PTPL1 is a non-receptor protein tyrosine phosphatase involved in apoptosis regulation, although controversial findings have been reported in different cancer types. We report here a proapoptotic role for PTPL1 in PC3 and LNCaP prostate cancer cells, as its absence induces apoptosis resistance upon treatment with different drugs. In PC3 cells, PTPL1 silencing by small interfering RNA influences the expression levels of Bcl-xL and Mcl-1(S) proteins as well as final events in the apoptotic process such as activation of caspases and caspase-mediated cleavage of proteins like Mcl-1 or poly (ADP-ribose) polymerase. We have identified PKCdelta as an intermediary of PTPL1-mediated apoptotic signalling and that phosphorylation status of NF-kappaB and IkappaBalpha is influenced by PTPL1 and PKCdelta. Furthermore, the loss of PTPL1 and PKCdelta expression in poorly differentiated, more aggressive human prostate cancers also indicate that their absence could be related to apoptosis resistance and tumour progression.
**TÍTULO / TITLE:** - Anti-Oxidative and Anti-Proliferative Activity on Human Prostate Cancer Cells Lines of the Phenolic Compounds from Corylopsis coreana Uyeki.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


- Enlace al texto completo (gratuito o de pago) 3390/molecules18054876

**AUTORES / AUTHORS:** - Kim MH; Ha SY; Oh MH; Kim HH; Kim SR; Lee MW

**INSTITUCIÓN / INSTITUTION:** - College of Pharmacy, Chung-Ang University, Seoul 156-756, Korea. mwlee@cau.ac.kr.

**RESUMEN / SUMMARY:** - Fifteen phenolic compounds, including three caffeoyl derivatives, four gallotannins, three ellagitannins and five flavonoids, were isolated from an 80% MeOH extract of the leaves of Corylopsis coreana Uyeki (Korean winter hazel; CL). The anti-oxidative activities [1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity and xanthine oxidase superoxide scavenging activities (NBT)] and the anti-proliferative activity on human prostate cancer cell lines (DU145 and LNCaP) were also evaluated.

**[1232]**

**TÍTULO / TITLE:** - Increasing Intracellular Bioavailable Copper Selectively Targets Prostate Cells.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


- Enlace al texto completo (gratuito o de pago) 1021/cb400198p

**AUTORES / AUTHORS:** - Cater MA; Pearson HB; Wolyniec K; Klaver P; Bilandzic M; Paterson BM; Bush Al; Humbert PO; La Fontaine S; Donnelly PS; Haupt Y

**INSTITUCIÓN / INSTITUTION:** - Research Division, Peter MacCallum Cancer Centre, East Melbourne, Victoria 3002, Australia.

**RESUMEN / SUMMARY:** - The therapeutic efficacy of two bis(thiosemicarbazone) copper complexes, glyoxalbis[N4-methylthiosemicarbazonato]CuII [CuII(gtsm)] and diacetylbis[N4-methylthiosemicarbazonato]CuII [CuII(atsm)], for the treatment of prostate cancer was assessed in cell culture and animal models. Distinctively, copper dissociates intracellularly from CuII(gtsm) but is retained by CuII(atsm). We further demonstrated that intracellular H2gtsm [reduced CuII(gtsm)] continues to redistribute copper into a bioavailable (exchangeable) pool. Both CuII(gtsm) and CuII(atsm) selectively kill transformed (hyperplastic and carcinoma) prostate cell lines but, importantly, do not affect the viability of primary prostate epithelial cells. Increasing extracellular copper concentrations enhanced the therapeutic capacity of both CuII(gtsm) and CuII(atsm), and their ligands (H2gtsm and H2atsm) were toxic only toward cancerous prostate cells when
combined with copper. Treatment of the Transgenic Adenocarcinoma of Mouse Prostate (TRAMP) model with CuII(gtsm) (2.5 mg/kg) significantly reduced prostate cancer burden (approximately 70%) and severity (grade), while treatment with CuII(atsm) (30 mg/kg) was ineffective at the given dose. However, CuII(gtsm) caused mild kidney toxicity in the mice, associated primarily with interstitial nephritis and luminal distention. Mechanistically, we demonstrated that CuII(gtsm) inhibits proteasomal chymotrypsin-like activity, a feature further established as being common to copper-ionophores that increase intracellular bioavailable copper. We have demonstrated that increasing intracellular bioavailable copper can selectively kill cancerous prostate cells in vitro and in vivo and have revealed the potential for bis(thiosemicarbazone) copper complexes to be developed as therapeutics for prostate cancer.

[1234]

**TITULO / TITLE:** Recruitment of mesenchymal stem cells into prostate tumours promotes metastasis.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Jung Y; Kim JK; Shiozawa Y; Wang J; Mishra A; Joseph J; Berry JE; McGee S; Lee E; Sun H; Wang J; Jin T; Zhang H; Dai J; Krebsbach PH; Keller ET; Pienta KJ; Taichman RS

**INSTITUCIÓN / INSTITUTION:** Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, Michigan 48109, USA.

**RESUMEN / SUMMARY:** Tumours recruit mesenchymal stem cells to facilitate healing, which induces their conversion into cancer-associated fibroblasts that facilitate metastasis. However, this process is poorly understood on the molecular level. Here we show that CXCL16, a ligand for CXCR6, facilitates mesenchymal stem cell or very small embryonic-like cells recruitment into prostate tumours. CXCR6 signalling stimulates the conversion of mesenchymal stem cells into cancer-associated fibroblasts, which secrete stromal-derived factor-1, also known as CXCL12. CXCL12 expressed by cancer-associated fibroblasts then binds to CXCR4 on tumour cells and induces an epithelial-to-mesenchymal transition, which ultimately promotes metastasis to secondary tumour sites. Our results provide the molecular basis for mesenchymal stem cell recruitment into tumours and how this process leads to tumour metastasis.

[1235]

**TITULO / TITLE:** Erratum to: Significance of IL-6 in the transition of hormone-resistant prostate cancer and the induction of myeloid-derived suppressor cells.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
TÍTULO / TITLE: - Multiple cytokeratin-negative malignant tumors composed only of rhabdoid cells in the renal pelvis: a sarcomatoid urothelial carcinoma?

RESUMEN / SUMMARY: - The author presents a unique case of multiple cytokeratin-negative malignant tumors consisting only of rhabdoid cells in the renal pelvis. A 54-year-old man complained of hematuria. A transurethral endoscopic examination revealed multiple papillary tumors, and transurethral resection of the bladder tumors was performed. Pathologically, they were ordinary papillary urothelial transitional cell carcinomas. Imaging modalities revealed multiple tumors of the right renal pelvis, and nephrectomy was performed. Grossly, three polypoid tumors measuring 2-4 cm were present in the pelvis. Histologically, they were composed only of malignant cells with rhabdoid features. There were no elements of transitional cell carcinoma. Immunohistochemically, the pelvic tumors were positive for vimentin and Ki-67 antigen (labeling=40%). They were negative for pancytokeratins (AE1/3, CAM5.2, KL-1 and polyclonal wide), 34betaE12, cytokeratin (CK) 5/6, CK7, CK8, CK14, CK18, CK19, CK20, melanosome, EMA, CEA, desmin, S100 protein, alpha-smooth muscle actin, myoglobin, myogenin, CD34, p53 protein, p63, CD3, CD20, CD30, CD45, CD45RO, chromograin, synaptophysin, CD56, CD68, and KIT. NSE and PDGFRA were focally present, but this appeared nonspecific. Namely, the pelvic tumors expressed only vimentin. The author speculates that the pelvic multiple malignant “rhabdoid” tumors are not sarcomas but urothelial “rhabdoid” carcinoma with complete loss of CKs.

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TÍTULO / TITLE: - Enoxacin inhibits growth of prostate cancer cells and effectively restores microRNA processing.

RESUMEN / SUMMARY: - Enoxacin inhibits growth of prostate cancer cells and effectively restores microRNA processing.
Prostate cancer (PCa) is one of the most incident malignancies worldwide. Although efficient therapy is available for early-stage PCa, treatment of advanced disease is mainly ineffective and remains a clinical challenge. microRNA (miRNA) dysregulation is associated with PCa development and progression. In fact, several studies have reported a widespread downregulation of miRNAs in PCa, which highlights the importance of studying compounds capable of restoring the global miRNA expression. The main aim of this study was to define the usefulness of enoxacin as an anti-tumoral agent in PCa, due to its ability to induce miRNA biogenesis in a TRBP-mediated manner. Using a panel of five PCa cell lines, we observed that all of them were wild type for the TARBP2 gene and expressed TRBP protein. Furthermore, primary prostate carcinomas displayed normal levels of TRBP protein. Remarkably, enoxacin was able to decrease cell viability, induce apoptosis, cause cell cycle arrest, and inhibit the invasiveness of cell lines. Enoxacin was also effective in restoring the global expression of miRNAs. This study is the first to show that PCa cells are highly responsive to the anti-tumoral effects of enoxacin. Therefore, enoxacin constitutes a promising therapeutic agent for PCa.

[1238]


RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Toivanen R; Frydenberg M; Murphy D; Pedersen J; Ryan A; Pook D; Berman DM; Taylor RA; Risbridger GP

INSTITUCIÓN / INSTITUTION: Department of Anatomy and Developmental Biology, Monash University, Clayton, Victoria 3800, Australia.

RESUMEN / SUMMARY: A lack of clinically relevant experimental models of human prostate cancer hampers evaluation of potential therapeutic agents. Currently, androgen deprivation therapy is the gold standard treatment for advanced prostate cancer, but inevitably, a subpopulation of cancer cells survives and repopulates the tumor. Tumor cells that survive androgen withdrawal are critical therapeutic targets for more effective treatments, but
current model systems cannot determine when they arise in disease progression and are unable to recapitulate variable patient response to treatment. A model system was developed in which stromal-supported xenografts from multiple patients with early-stage localized disease can be tested for response to castration. The histopathology of these xenografts mimicked the original tumors, and short-term host castration resulted in reduced proliferation and increased apoptosis in tumor cells. After 4 weeks of castration, residual populations of quiescent, stem-like tumor cells remained. Without subsequent treatment, these residual cells displayed regenerative potential, because testosterone readministration resulted in emergence of rapidly proliferating tumors. Therefore, this model may be useful for revealing potential cellular targets in prostate cancer, which exist before the onset of aggressive incurable disease. Specific eradication of these regenerative tumor cells that survive castration could then confer survival benefits for patients.

[1239]

**TÍTULO / TITLE:** - Carbonic anhydrase IX from cancer-associated fibroblasts drives epithelial-mesenchymal transition in prostate carcinoma cells.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Cell Cycle. 2013 May 8;12(11).

**AUTORES / AUTHORS:** - Fiaschi T; Giannoni E; Taddei ML; Cirri P; Marini A; Pintus G; Nativi C; Richichi B; Scozzafava A; Carta F; Torre E; Supuran CT; Chiarugi P

**INSTITUCIÓN / INSTITUTION:** - Department of Biomedical, Experimental and Clinical Sciences; University of Florence, Tuscany; Tumor Institute and “Center for Research, Transfer and High Education DenoTHE”; Florence, Italy.

**RESUMEN / SUMMARY:** - Extracellular acidification, a mandatory feature of several malignancies, has been mainly correlated with metabolic reprogramming of tumor cells toward Warburg metabolism, as well as to the expression of carbonic anydrases or proton pumps by malignant tumor cells. We report herein that for aggressive prostate carcinoma, acknowledged to be reprogrammed toward an anabolic phenotype and to upload lactate to drive proliferation, extracellular acidification is mainly mediated by stromal cells engaged in a molecular cross-talk circuitry with cancer cells. Indeed, cancer-associated fibroblasts, upon their activation by cancer delivered soluble factors, rapidly express carbonic anhydrase IX (CA IX). While expression of CAIX in cancer cells has already been correlated with poor prognosis in various human tumors, the novelty of our findings is the upregulation of CAIX in stromal cells upon activation. The de novo expression of CA IX, which is not addicted to hypoxic conditions, is driven by redox-based stabilization of hypoxia-inducible factor-1. Extracellular acidification due to carbonic anhydrase IX is mandatory to elicit activation of stromal fibroblasts delivered metalloprotease-2 and -9, driving in cancer cells the epithelial-mesenchymal transition epigenetic program, a key
event associated with increased motility, survival and stemness. Both genetic silencing and pharmacological inhibition of CA IX (with sulfonamide/sulfamides potent inhibitors) or metalloprotease-9 are sufficient to impede epithelial-mesenchymal transition and invasiveness of prostate cancer cells induced by contact with cancer-associated fibroblasts. We also confirmed in vivo the upstream hierarchical role of stromal CA IX to drive successful metastatic spread of prostate carcinoma cells. These data include stromal cells, as cancer-associated fibroblasts as ideal targets for carbonic anhydrase IX-directed anticancer therapies.

[1240]
**TÍTULO / TITLE:** Expression of Cancer/Testis Antigens is Correlated with Improved Survival in Glioblastoma.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Freitas M; Malheiros S; Stavale JN; Biassi TP; Zamuner FT; de Souza Begnami M; Soares FA; Vettore AL

**INSTITUCIÓN / INSTITUTION:** Cancer Molecular Biology Laboratory, Department of Science Biology, Federal University of Sao Paulo, Rua Pedro de Toledo, Sao Paulo, SP, Brazil.

**RESUMEN / SUMMARY:** Background: Glioblastoma (GBM) confers a dismal prognosis despite advances in current therapy. Cancer-testis antigens (CTA) comprise families of tumor-associated antigens that are immunogenic in different cancers. The aim of this study was to determine the expression profile of a large number of CTA genes in GBM. Methods: We selected, from 153 CTA genes, those genes potentially expressed in GBM. The expression pattern of 30 CTA was then evaluated by RT-PCR in a series of 48 GBM and 5 normal brain samples. The presence of CTCFL protein was also evaluated by immunohistochemical staining. Results: Among the genes with no expression in normal brain, ACTL8 (57%), OIP5 (54%), XAGE3 (44%) and CTCFL (15%) were frequently expressed in GBM, while over 85% of the tumors expressed at least 1 of these four CTA. Coexpression of two or more CTA occurred in 49% of cases. CTCFL protein expression was detected in 13% of the GBM and was negative in normal brain samples. GBM expressing 3-4 CTA was associated with significantly better overall survival (OS) rates (P = 0.017). By multivariate analysis, mRNA positivity for 3-4 CTA (P = 0.044), radiotherapy (P = 0.010) and chemotherapy (P = 0.001) were independent prognostic factors for OS. Conclusions: GBM frequently express ACTL8, OIP5, XAGE3 and CTCFL. A relatively high percentage of tumors expressed at least one of these four CTA, opening the perspective for their utility in antigen-specific immunotherapy. Furthermore, mRNA positivity for 3-4 CTA is an independent predictor of better OS for GBM patients.
TÍTULO / TITLE: - Celastrol suppresses tumor cell growth through targeting an AR-ERG-NF-kappaB pathway in TMPRSS2/ERG fusion gene expressing prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Shao L; Zhou Z; Cai Y; Castro P; Dakhov O; Shi P; Bai Y; Ji H; Shen W; Wang J

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Immunology, Baylor College of Medicine and Michael E. DeBakey Department of Veterans Affairs Medical Center, Houston, Texas, USA.

RESUMEN / SUMMARY: - The TMPRSS2/ERG (T/E) fusion gene is present in the majority of all prostate cancers (PCa). We have shown previously that NF-kB signaling is highly activated in these T/E fusion expressing cells via phosphorylation of NF-kB p65 Ser536 (p536). We therefore hypothesize that targeting NF-kB signaling may be an efficacious approach for the subgroup of PCAs that carry T/E fusions. Celastrol is a well known NF-kB inhibitor, and thus may inhibit T/E fusion expressing PCa cell growth. We therefore evaluated Celastrol's effects in vitro and in vivo in VCaP cells, which express the T/E fusion gene. VCaP cells were treated with different concentrations of Celastrol and growth inhibition and target expression were evaluated. To test its ability to inhibit growth in vivo, 0.5 mg/kg Celastrol was used to treat mice bearing subcutaneous VCaP xenograft tumors. Our results show Celastrol can significantly inhibit the growth of T/E fusion expressing PCa cells both in vitro and in vivo through targeting three critical signaling pathways: AR, ERG and NF-kB in these cells. When mice received 0.5 mg/kg Celastrol for 4 times/week, significant growth inhibition was seen with no obvious toxicity or significant weight loss. Therefore, Celastrol is a promising candidate drug for T/E fusion expressing PCa. Our findings provide a novel strategy for the targeted therapy which may benefit the more than half of PCa patients who have T/E fusion expressing PCAs.

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TÍTULO / TITLE: - Understanding variation in the quality of the surgical treatment of prostate cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Shao L; Zhou Z; Cai Y; Castro P; Dakhov O; Shi P; Bai Y; Ji H; Shen W; Wang J

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Immunology, Baylor College of Medicine and Michael E. DeBakey Department of Veterans Affairs Medical Center, Houston, Texas, USA.

RESUMEN / SUMMARY: - Understanding variation in the quality of the surgical treatment of prostate cancer.
AUTORES / AUTHORS: - Schroeck FR; Jacobs BL; Hollenbeck BK
INSTITUCIÓN / INSTITUTION: - From the Divisions of Health Services Research and Urologic Oncology, Department of Urology, University of Michigan, Ann Arbor, MI.
RESUMEN / SUMMARY: - More than 80% of men with prostate cancer undergo active treatment, which can be associated with significant morbidity. Outcomes of surgical treatment vary widely depending on who treated the patient and where the patient was treated, implying that there is room for improvement. Factors influencing outcomes include patient characteristics as well as some measure of procedure volume. Although relationships between volume and outcomes for prostatectomy can most likely be explained by differences between surgeons (e.g., experience, technical skill), the hospital environment (e.g., team communication, safety culture) has the potential to either amplify or dampen the effects. Although most patient factors are immutable, these other aspects of surgical care and the delivery environment provide opportunities for quality improvement. Collaborative quality improvement initiatives may prove to be an important vehicle for achieving better prostate cancer care. These grass roots organizations, driven largely by urologists dedicated to providing prostate cancer care, have had initial successes in improving some aspects of quality in prostate cancer care, including reducing unwarranted use of imaging and perioperative morbidity. However, much of the variation in functional outcomes after prostate cancer surgery arises from differences in technical skill. Evaluating and improving intraoperative surgeon performance will inevitably be challenging, as they require acquisition and interpretation of data collected in the operating room. To this end, several methods have been described to objectively assess what happens in the operating room.

[1243]
TITULO / TITLE: - Long-term outcome for prostate cancer using pseudo pulse-dosed rate brachytherapy, external beam radiotherapy, and hormones.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Izard MA; Morris LM; Wan WY; Martin J
INSTITUCIÓN / INSTITUTION: - Department of Radiotherapy, Mater Hospital, North Sydney, New South Wales, Australia; Northern Clinical School, University of Sydney, New South Wales, Australia. Electronic address: michael.izard@cancer.com.au.
RESUMEN / SUMMARY: - PURPOSE: We report the long-term outcomes of pulse-dose rate (PDR) brachytherapy used in a nonstandard style (pseudo-PDR) with an high-dose rate brachytherapy technique in conjunction with external beam...
METHODS AND MATERIALS: We treated 253 patients with Stage T1-T3 N0M0 PC, between December 1999 and March 2006. All patients received neoadjuvant androgen deprivation for a median 6 months. Treatment consisted of three pulses of pseudo-PDR brachytherapy to a median dose of 18Gy with 50.4Gy in 28 fractions of EBRT. RESULTS: At a median 6 years followup, (range, 1-11 years), 5-year overall survival was 92%, and PC-specific survival was 96%. The 5-year biochemical control (biochemical no evidence of disease) by the Phoenix definition for low-, intermediate-, and high-risk groups was 95%, 90%, and 71%, respectively (p<0.00001). At 6 years, the incidence of Radiotherapy Oncology Group Grade 2 and 3 genitourinary toxicity was 1% and 6%; Radiotherapy Oncology Group Grade 2 and 3 gastrointestinal toxicity was 4% and 0%. Erectile preservation at 3 years was 58%. The Phoenix definition best predicted clinical failure with a high specificity (94%). CONCLUSIONS: Pseudo-PDR brachytherapy plus EBRT with limited neoadjuvant hormonal manipulation is an effective treatment option in localized PC, with minimal and tolerable morbidity and provides excellent control. This technique of a modified PDR-delivery technique appears as effective as high-dose rate therapy.

[1244]

**TÍTULO / TITLE:** Epigenetic Modifications of Nrf2 by 3,3'-diindolylmethane In Vitro in TRAMP C1 Cell Line and In Vivo TRAMP Prostate Tumors.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** AAPS J. 2013 May 9.

**ENLACE AL TEXTO COMPLETO (GRATUITO O DE PAGO):** 1208/s12248-013-9493-3

**AUTORES / AUTHORS:** Wu TY; Khor TO; Su ZY; Saw CL; Shu L; Cheung KL; Huang Y; Yu S; Kong AN

**INSTITUCIÓN / INSTITUTION:** Center for Cancer Prevention Research, Department of Pharmaceutics, Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, Room 228, 160 Frelinghuysen Road, Piscataway, New Jersey, 08854, USA.

**RESUMEN / SUMMARY:** 3,3'-diindolylmethane (DIM) is currently being investigated in many clinical trials including prostate, breast, and cervical cancers and has been shown to possess anticancer effects in several in vivo and in vitro models. Previously, DIM has been reported to possess cancer chemopreventive effects in prostate carcinogenesis in TRAMP mice; however, the in vivo mechanism is unclear. The present study aims to investigate the in vitro and in vivo epigenetics modulation of DIM in TRAMP-C1 cells and in TRAMP mouse model. In vitro study utilizing TRAMP-C1 cells showed that DIM suppressed DNMT expression and reversed CpG methylation status of Nrf2 resulting in enhanced expression of Nrf2 and Nrf2-target gene NQO1. In vivo study, TRAMP mice fed with DIM-supplemented diet showed much lower
incidence of tumorigenesis and metastasis than the untreated control group similar to what was reported previously. DIM increased apoptosis, decreased cell proliferation and enhanced Nrf2 and Nrf2-target gene NQO1 expression in prostate tissues. Importantly, immunohistochemical analysis showed that DIM reduced the global CpG 5-methylcytosine methylation. Focusing on one of the early cancer chemopreventive target gene Nrf2, bisulfite genomic sequencing showed that DIM decreased the methylation status of the first five CpGs of the Nrf2 promoter region, corroborating with the results of in vitro TRAMP-C1 cells. In summary, our current study shows that DIM is a potent cancer chemopreventive agent for prostate cancer and epigenetic modifications of the CpG including Nrf2 could be a potential mechanism by which DIM exerts its chemopreventive effects.

[1245]
TÍTULO / TITLE: - In Vitro and In Vivo (1)H-MR Spectroscopic Examination of the Renal Cell Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Sullentrop F; Hahn J; Moka D
INSTITUCIÓN / INSTITUTION: - Institute of Inorganic Chemistry and the Department of Nuclear Medicine University of Cologne, Germany.
RESUMEN / SUMMARY: - BACKGROUND: Paraneoplastic effects are some of the major side effects of advanced renal cell carcinoma (RCC). Magnetic resonance spectroscopy (MRS) is known as a powerful tool to study cancer cell metabolism and cancer cell-host interactions. Aim of this study was to assess tumor cell metabolism and systemic effects using (1)H-MRS. METHODS: Spectroscopic analysis of 10 patients with RCC was compared with those of 15 healthy volunteers. Local tumor metabolism was assessed using image-guided (1)H-in-vivo-spectroscopy in a 1.5 Tesla MR whole body tomograph. Systemic effects of RCC were measured using (1)H-High-Resolution (HR) spectra of blood plasma samples in a 500 MHz Bruker DRX 500 spectrometer. RESULTS: In-vivo-spectroscopy can significantly differentiate tumor tissue from healthy renal tissue by comparing their lipid composition. Moreover after detailed assignment of the various metabolites in blood plasma in the in-vitro-HR-spectra significant systemic alterations could be identified in patients with RCC especially regarding lipid and amino acid metabolism. CONCLUSION: This work indicates that using (1)H-MRS both changes in tumor metabolism and resulting systemic/paraneoplastic effects can be assessed in patients with RCC. This approach therefore offers scope for diagnosis and therapy evaluation.

[1246]
TÍTULO / TITLE: - Transurethral resection of bladder tumour (TURBT) as an optional treatment method on pheochromocytoma of the urinary bladder.
Pheochromocytoma of the urinary bladder is rare. We have experienced a case of unexpected pheochromocytoma of the urinary bladder in a 45-year-old female. An ultrasonographic, computed tomography scan and cystoscopic examination showed a submucosal bladder mass. After transurethral resection of bladder tumour was performed, the bladder mass was confirmed as pheochromocytoma by a pathologist. After surgery, the patient underwent a subsequent pelvic magnetic resonance imaging, positron emission tomography and I(131)-methylidobenzylguanidine (I(131)-MIBG). An image study showed no residual tumour sites and no lymphatic metastasis. The patient has had no tumour recurrence and no voiding symptoms 3 years after the surgery.

Background: Prostate cancer is the most commonly diagnosed cancer in men in Europe and the United States. Numerous studies have indicated genetics to have a major role in the aetiology of this disease; as much as 42% of the risk may be explained by heritable factors. Genome-wide association studies have detected an association between prostate cancer and chromosome 8p21-23. In this study, we analysed eight microsatellite (MS) markers in that region in order to confirm previous results and narrow down the location of candidate prostate cancer genes.

Methods: 292 cases and 278
controls were selected from the Netherlands Cohort Study (NLCS). The following MSs were used in the analyses: D8S136, D8S1734, D8S1742, D8S261, D8S262, D8S351, D8S511 and D8S520. Associations were evaluated using a chi2 test and logistic regression. We checked for any effects on the association by tumour stage. Results: Associations that were found confirmed previous research that pointed to the 8p21-23 region. Two MSs: D8S136 (odds ratio (OR), 0.69; P=4.00 x 10^-28), and D8S520 (OR, 0.80; P=3.37 x 10^-11), were consistently and strongly related with prostate cancer. Genotype analysis showed an additive effect for D8S136 (P-trend=6.22 x 10^-03) and D8S520 (P-trend=2.62 x 10^-22), suggesting an increased risk for people with a short number of repeats on both alleles at those markers. Conclusions: This study provides strong evidence that the 8p21-23 region is likely to harbour prostate cancer genes.

Prostate Cancer and Prostatic Disease advance online publication, 30 April 2013; doi:10.1038/pcan.2013.9.

[1248]

TÍTULO / TITLE: - Prostate derived Ets transcription factor and Carcinoembryonic antigen related cell adhesion molecule 6 constitute a highly active oncogenic axis in breast cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Mukhopadhyay A; Khoury T; Stein L; Shrikant P; Sood AK

INSTITUCIÓN / INSTITUTION: - Department of Immunology, Roswell Park Cancer Institute, Buffalo, NY.

RESUMEN / SUMMARY: - We previously reported overexpression of Prostate derived Ets transcription factor (PDEF) in breast cancer and its role in breast cancer progression, supporting PDEF as an attractive target in this cancer. The goal of this research was to identify specific PDEF induced molecules that, like PDEF, show overexpression in breast tumors and a role in breast tumor progression. PDEF expression was down regulated by shRNA in MCF-7 human breast tumor cell line, and probes from PDEF down-regulated and control MCF-7 cells were used to screen the HG-U133A human gene chips. These analyses identified 1318 genes that were induced two-fold or higher by PDEF in MCF-7 cells. Further analysis of three of these genes, namely CEACAM6, S100A7 and B7-H4, in relation to PDEF in primary breast tumors showed that in 82% of ER+, 67% of Her2 overexpressing and 24% of triple-negative breast tumors both PDEF and CEACAM6 expression was elevated 10-fold or higher in comparison to normal breast tissue. Overall, 72% (94 of 131) of the primary breast tumors showed 10-fold or higher expression of both PDEF and CEACAM6. In contrast, S100A7 and B7-H4 failed to show concordant elevated expression with PDEF in primary tumors. To determine the significance of elevated PDEF and CEACAM6 expression to tumor phenotype, their expression...
was down regulated by specific siRNAs in human breast tumor cell lines. This resulted in the loss of viability of tumor cells in vitro, supporting an oncogenic role for both PDEF and CEACAM6 in breast cancer. Together, these findings show that PDEF-CEACAM6 is a highly active oncogenic axis in breast cancer and suggest that targeting of these molecules should provide novel treatments for most breast cancer patients.

[1249]

_TÍTULO / TITLE:_ Targeting bone physiology for the treatment of metastatic prostate cancer.

_RESUMEN / SUMMARY:_ Enlace al Resumen / Link to its Summary


_AUTORES / AUTHORS:_ Autio KA; Morris MJ

_INSTITUCIÓN / INSTITUTION:_ Memorial Sloan-Kettering Cancer Center, New York, New York 10065, USA.

_RESUMEN / SUMMARY:_ Metastatic prostate cancer has a unique predilection for bone that can lead to significant clinical sequelae, such as fracture and cord compression. This tropism for bone yields not only clinical challenges, but also opportunities to understand the tumor biology in bone and to develop relevant therapeutic strategies. The process by which tumor cells migrate to bone, remain dormant, and then colonize and expand is based on complex interactions between prostate cancer tumor cells and the host microenvironment. This review will provide an overview of these interactions as well as therapies targeting osseous metastases in castration-resistant prostate cancer.

[1250]

_TÍTULO / TITLE:_ Increased expression of pregnancy up-regulated non-ubiquitous calmodulin kinase is associated with poor prognosis in clear cell renal cell carcinoma.

_RESUMEN / SUMMARY:_ Enlace al Resumen / Link to its Summary


_AUTORES / AUTHORS:_ Wu S; Lv Z; Wang Y; Sun L; Jiang Z; Xu C; Zhao J; Sun X; Li X; Hu L; Tang A; Gui Y; Zhou F; Cai Z; Wang R

_INSTITUCIÓN / INSTITUTION:_ Institute of Immunology, Zhongshan School of Medicine, Sun Yat-sen University, Guangzhou, Guangdong, China; Shenzhen Second People’s Hospital, The First Affiliated Hospital of Shenzhen University, Shenzhen, Guangdong, China; Department of Urology, Sun Yat-Sen University Cancer Center, Guangzhou, Guangdong, China.
RESUMEN / SUMMARY: - PURPOSE: The aims of this study were to evaluate the clinical significance and potential prognostic value of pregnancy up-regulated non-ubiquitous calmodulin kinase (PNCK) in clear cell renal cell carcinoma (ccRCC) patients. MATERIALS AND METHODS: The expression of PNCK mRNA was determined in 24 paired samples of ccRCCs and adjacent normal tissues using real-time RT-PCR. The expression of PNCK was determined in 248 samples of ccRCCs and 92 paired samples of adjacent normal tissues by immunohistochemical analysis. Statistical analysis was performed to define the relationship between PNCK expression and the clinical features of ccRCC. RESULTS: The mRNA level of PNCK was significantly higher in tumorous tissues than in the adjacent non-tumorous tissues (p<0.001). An immunohistochemical analysis of 92 paired tissue specimens showed that PNCK expression was higher in tumorous tissues than in the adjacent non-tumorous tissues (p<0.001). Moreover, there was a significant correlation between the PNCK expression and various clinicopathological parameters such as Fuhrman grade (p = 0.011), tumor size (p<0.001), T stage (p<0.001) and N stage (p = 0.015). Patients with higher PNCK expression had shorter overall survival time than those with lower PNCK expression (p<0.001). Multivariate analysis indicated that PNCK expression was an independent predictor for poor survival of ccRCC patients. CONCLUSIONS: To our knowledge, this is the first study that determines the relationship between PNCK and prognosis in ccRCC. We found that increased PNCK expression is associated with poor prognosis in ccRCC. PNCK may represent a novel prognostic marker for ccRCC.

[1251]
TÍTULO / TITLE: - Sutureless Hemostatic Control During Laparoscopic NSS for the Treatment of Small Renal Masses.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Minervini A; Siena G; Tuccio A; Lapini A; Serni S; Carini M
INSTITUCIÓN / INSTITUTION: - 1University of Florence, Careggi Hospital, Florence, Italy.
RESUMEN / SUMMARY: - Background. This study aimed to evaluate the safety and efficacy of a sutureless hemostatic control during laparoscopic nephron sparing surgery (LNSS) for the treatment of small renal masses. Methods. Between November 2007 and August 2010, 245 patients underwent nephron sparing surgery. Overall, 100 patients (41%) had LNSS. Hemostasis was controlled either by a knot-tying suture repair (standard-LNSS) or by a sutureless technique (s-LNSS). The s-LNSS was done using a bipolar cauterization of the resection bed, followed by Floseal apposition. Operative
and warm ischemia time (WIT), intraoperative blood loss, hospital stay, blood tests, and perioperative complications were recorded. Results. In 32 cases (32%) hemostasis was controlled by the sutureless technique. The s-LNSS was the treatment of choice for small tumors ≤=1.5 cm, and it was also used for the treatment of tumors between 1.6 and 2.5 cm, aside from their spatial extension. Indeed, the mean (range; interquartile range) clinical dimension of the tumors in the s-LNSS group was 1.9 (1-3.5; 1.5-2.1) cm. On the contrary, the vast majority of tumors >2.5 cm were treated with standard-LNSS. Mean (range; interquartile range) WIT in the s-LNSS group was 16 (8-22; 12-16) minutes. The mean (range) intraoperative blood loss in the s-LNSS group was 107 cc (25-205). No postoperative early and late bleeding were reported in the s-LNSS group, and the mean (range) time to drainage removal and time to discharge were 3 (2-5) and 4 (3-7) days, respectively. Conclusions. The sutureless technique with bipolar cauteryization of the surgical bed and Floseal apposition is safe and effective for the hemostatic control in the treatment of small cortical masses. It can be always used for tumors ≤=1.5 cm and can be a valid option also for tumors between 1.6 and 2.5 cm, aside from their spatial extension.

[1252]

TÍTULO / TITLE: - Interferon-alpha Treatment for Growing Teratoma Syndrome of the Testis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Inoue M; Hisasue S; Nagae M; China T; Saito K; Isotani S; Yamaguchi R; Ide H; Muto S; Horie S

INSTITUCIÓN / INSTITUTION: - Department of Urology, Teikyo University School of Medicine, Tokyo, Japan.

RESUMEN / SUMMARY: - A 23-year-old man with a right scrotal mass and back pain was referred for further treatment after right radical orchiectomy for testicular cancer. CT scans brought by the patient showed extensive metastasis to the retroperitoneal lymph nodes with no lung involvement. alpha-Fetoprotein and human chorionic gonadotropin were elevated preoperatively (384 ng/ml and 112 mIU/ml, respectively). Confirmation of the histopathologic examination revealed a mixed germ cell tumor (95% immature teratoma and 5% embryonal carcinoma). We started the patient on chemotherapy with bleomycin, etoposide, and cisplatin (BEP). After a single course, tumor markers began to normalize, but there was radiologic evidence of continued growth of the retroperitoneal mass and new metastases in the lung. The patient was given 2 courses of salvage chemotherapy with etoposide, ifosfamide, and cisplatin (VIP). However, the mass and lung metastases continued to progress, and the patient was growing rapidly intolerant of the side effects of treatment (i.e., nausea, appetite
loss, and pancytopenia). After thorough discussion with the patient and his family, we decided to start the patient on interferon (IFN)-alpha therapy. Natural, nonrecombinant IFN-alpha (OIF, Otsuka, Japan) 5,000,000 IU was administered twice weekly with approval of the ethics committee of our institution. The patient responded moderately with marked deceleration of tumor growth and stabilization of the lung metastases. He is alive and well at 16 months on IFN-alpha therapy.

[1253]

**TITULO / TITLE:** - Low-dose-rate or high-dose-rate brachytherapy in treatment of prostate cancer - between options.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Skowronek J

**INSTITUCION / INSTITUTION:** - Brachytherapy Department, Greater Poland Cancer Center, Poznan, Poland.

**RESUMEN / SUMMARY:** - PURPOSE: Permanent low-dose-rate (LDR-BT) and temporary high-dose-rate (HDR-BT) brachytherapy are competitive techniques for clinically localized prostate radiotherapy. Although a randomized trial will likely never to be conducted comparing these two forms of brachytherapy, a comparative analysis proves useful in understanding some of their intrinsic differences, several of which could be exploited to improve outcomes. The aim of this paper is to look for possible similarities and differences between both brachytherapy modalities. Indications and contraindications for monotherapy and for brachytherapy as a boost to external beam radiation therapy (EBRT) are presented. It is suggested that each of these techniques has attributes that advocates for one or the other. First, they represent the extreme ends of the spectrum with respect to dose rate and fractionation, and therefore have inherently different radiobiological properties. Low-dose-rate brachytherapy has the great advantage of being practically a one-time procedure, and enjoys a long-term follow-up database supporting its excellent outcomes and low morbidity. Low-dose-rate brachytherapy has been a gold standard for prostate brachytherapy in low risk patients since many years. On the other hand, HDR is a fairly invasive procedure requiring several sessions associated with a brief hospital stay. Although lacking in significant long-term data, it possesses the technical advantage of control over its postimplant dosimetry (by modulating the source dwell time and position), which is absent in LDR brachytherapy. This important difference in dosimetric control allows HDR doses to be escalated safely, a flexibility that does not exist for LDR brachytherapy. CONCLUSIONS: Radiobiological models support the current clinical evidence for equivalent outcomes in localized prostate cancer with either LDR or HDR brachytherapy,
using current dose regimens. At present, all available clinical data regarding these two techniques suggests that they are equally effective, stage for stage, in providing high tumor control rates.

[1254]

**TÍTULO / TITLE:** Regional treatment margins for prostate brachytherapy.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Jastaniyah N; Sloboda R; Kamal W; Moore H; Ghosh S; Pervez N; Pedersen J; Yee D; Danielson B; Murtha A; Amanie J; Usmani N

**INSTITUCIÓN / INSTITUTION:** Department of Oncology, University of Alberta, Edmonton, Alberta, Canada.

**RESUMEN / SUMMARY:** PURPOSE: This study quantified the treatment margin around the prostate that received 100% of the prescribed dose and analyzed postimplant dosimetry in different regions of the prostate for 125I seed implants.

**METODOS AND MATERIALS:** An average target volume (ATV) was created from postoperative MRI scan contours drawn independently by five radiation oncologists in 40 patients. The MRI was fused with the postoperative CT for dosimetry purposes. The TM, defined as the radial distance between the ATV and the 100% isodose line, was measured at 16 points at the base, midgland, and apex. The ATV was divided into four quadrants: anterior-superior, posterior-superior, anterior-inferior, and posterior-inferior quadrants. The values of the dose that covers 90% of the ATV (D90) and the percentage of the ATV receiving the prescribed dose (V100) were documented. RESULTS: The range of the mean TM, in millimeter, was -8.88 to 3.68, 1.12 to 10.42, and 6.27 to 18.25 at the base, midgland, and apex, respectively. The mean D90 was 135.8, 162.8, 191.0, and 194.6 Gy for the anterior-superior, posterior-superior, anterior-inferior, and posterior-inferior quadrants, respectively. CONCLUSIONS: Despite having a relatively uniform preoperative planning target volume, this study identified variable TMs postoperatively in different regions of the prostate. In particular, the anterior base is most underdosed, whereas the lateral regions of the midgland and apex have generous TMs. Postimplant dosimetric parameters were lowest in the anterior-inferior quadrant.

[1255]

**TÍTULO / TITLE:** Ongoing debate on the management of small renal masses: should they be treated like low-risk prostate cancers?

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
Maximizing dosimetric benefits of IMRT in the treatment of localized prostate cancer through multicriteria optimization planning.

We examine the quality of plans created using multicriteria optimization (MCO) treatment planning in intensity-modulated radiation therapy (IMRT) in treatment of localized prostate cancer. Nine random cases of patients receiving IMRT to the prostate were selected. Each case was associated with a clinically approved plan created using Corvus. The cases were replanned using MCO-based planning in RayStation. Dose-volume histogram data from both planning systems were presented to 2 radiation oncologists in a blinded evaluation, and were compared at a number of dose-volume points. Both physicians rated all 9 MCO plans as superior to the clinically approved plans (p<10-5). Target coverage was equivalent (p = 0.81). Maximum doses to the prostate and bladder and the V50 and V70 to the anterior rectum were reduced in all MCO plans (p<0.05). Treatment planning time with MCO took approximately 60 minutes per case. MCO-based planning for prostate IMRT is efficient and produces high-quality plans with good target homogeneity and sparing of the anterior rectum, bladder, and femoral heads, without sacrificing target coverage.

The histology of prostate tissue following prostatic artery embolization for the treatment of benign prostatic hyperplasia.

We examine the quality of plans created using multicriteria optimization (MCO) treatment planning in intensity-modulated radiation therapy (IMRT) in treatment of localized prostate cancer. Nine random cases of patients receiving IMRT to the prostate were selected. Each case was associated with a clinically approved plan created using Corvus. The cases were replanned using MCO-based planning in RayStation. Dose-volume histogram data from both planning systems were presented to 2 radiation oncologists in a blinded evaluation, and were compared at a number of dose-volume points. Both physicians rated all 9 MCO plans as superior to the clinically approved plans (p<10-5). Target coverage was equivalent (p = 0.81). Maximum doses to the prostate and bladder and the V50 and V70 to the anterior rectum were reduced in all MCO plans (p<0.05). Treatment planning time with MCO took approximately 60 minutes per case. MCO-based planning for prostate IMRT is efficient and produces high-quality plans with good target homogeneity and sparing of the anterior rectum, bladder, and femoral heads, without sacrificing target coverage.
Objective: Prostatic artery embolization (PAE) for the treatment of patients with symptomatic benign prostatic hyperplasia (BPH) is believed to be a safe procedure with a low risk of adverse side effects. Artery embolization is a viable treatment option in patients who are refractory to the classic noninvasive treatments. Knowledge of the histological characteristics of prostate tissue following the procedure is still limited. In this study, we describe the microscopic aspects of the prostate following PAE for BPH. Materials and Methods: Two patients underwent transurethral resections of the prostate (TURP) after PAE. Embolizations were performed under local anesthesia with an initial pelvic angiography to evaluate the iliac vessels and the prostate arteries using a 2.8 French microcatheter. The prostate was embolized with 300-500 microm Microspheres (Embosphere®), using complete blood stasis as the end point. The prostate tissues were analyzed histologically to characterize the effects of the embolization. Results: The embolic material within the prostate tissue was easily identified as homogeneous, bright eosin-red spheroids filling the vessel lumens. Ischemic necrosis surrounded or not by chronic inflammatory reactions containing macrophages were considered as a result of the artery embolization. Also, some aspects related to the healing process were observed being fibrotic nodules surrounded by glands with squamous metaplasia of the epithelial lining the most important. In the remaining sections, due to the precocious surgical intervention, the classic findings of BPH were still present with the glandular and stromal hyperplasia associated with nonspecific chronic prostatitis. Conclusions: This is the first description of prostate histology in BPH patients treated by PAE, a new procedure that is being used increasingly as a therapeutic intervention. The recognition of the changes caused by this new modality of treatment has become a very important differential in a chronic granulomatous reaction of the prostate tissue.

[1258]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Rick FG; Block NL; Schally AV

INSTITUCIÓN / INSTITUTION: - Endocrine, Polypeptide, and Cancer Institute, Veterans Affairs Medical Center and South Florida Veterans Affairs Foundation for Research and Education, University of Miami, Miller School of Medicine, Miami, Florida, USA.
RESUMEN / SUMMARY: - Androgen deprivation therapy remains the mainstay of medical treatment for advanced prostate cancer. Commonly, this is achieved with medical androgen deprivation rather than surgical intervention as the permanence and psychological effects of the latter are unacceptable for most patients. Degarelix is a third generation antagonist of luteinizing hormone-releasing hormone (LHRH, also termed gonadotropin-releasing hormone) for the first-line treatment of androgen-dependent advanced prostate cancer. Degarelix acts directly on the pituitary receptors for LHRH, blocking the action of endogenous LHRH. The use of degarelix eliminates the initial undesirable surge in gonadotropin and testosterone levels, which is produced by agonists of LHRH. Degarelix is the most comprehensively studied and widely available LHRH antagonist worldwide. Clinical trials have demonstrated that degarelix has a long-term efficacy similar to the LHRH agonist leuprolide in achieving testosterone suppression in patients with prostate cancer. Degarelix, however, produces a faster suppression of testosterone and prostate-specific antigen (PSA), with no testosterone surges or microsurges, and thus prevents the risk of clinical flare in advanced disease. Recent clinical trials demonstrated that treatment with degarelix results in improved disease control when compared with an LHRH agonist in terms of superior PSA progression-free survival, suggesting that degarelix likely delays progression to castration-resistant disease and has a more significant impact on bone serum alkaline phosphatase and follicle-stimulating hormone. Degarelix is usually well tolerated, with limited toxicity and no evidence of systemic allergic reactions in clinical studies. Degarelix thus represents an important addition to the hormonal armamentarium for therapy of advanced androgen-dependent prostate cancer.

[1259]

TÍTULO / TITLE: - The Treatment of Recurrent Urothelial Tumors of the Upper Urinary System and at Urostomy Site following Radical Cystectomy with Intraureteral Bacillus Calmette-Guerin and Cryotherapy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Demirtas A; Yildirim YE; Ferahbas A; Akinsal EC; Ekmekcioglu O; Tatlisen A

INSTITUCIÓN / INSTITUTION: - Department of Urology, Erciyes University Medical Faculty, 38039 Kayseri, Turkey.

RESUMEN / SUMMARY: - Urinary bladder carcinoma is the second most common cancer of the urinary system. The recurrence rate in the upper urinary system (UUS) for urothelial cancers is around 3% following radical cystectomy. The followup generally consists of imaging studies and urinary cytology, although there are no prospective data on the frequency, the mode, and the duration of
followup. In patients carefully selected according to risk factors, kidney-sparing minimally invasive methods (ureteroscopic procedures, percutaneous approach, and local drug instillation) appear as contemporary alternatives for low-grade and low-stage primary UUS. In this paper, we present the patient who underwent radical cystectomy with urinary diversion ureterocutaneostomy, was diagnosed with widespread bilateral UUS tumors and recurrent tumor at the urostomy site at active followup, for which he was given local Bacillus Calmette-Guerin (BCG) and cryotherapy, and was followed by disease-free for 2 years thereafter.

[1260]
TÍTULO / TITLE: - Is there an optimal treatment sequencing strategy for metastatic castration-resistant prostate cancer?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

[1261]
TÍTULO / TITLE: - The type of lymphocyte infiltration near urothelial carcinoma is diagnostic for chronic lymphocytic leukemia.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

[1262]
**TÍTULO / TITLE:** - FDG PET/CT in Prostate Cancer: A Valuable Method to Detect the Primary and Metastatic Tumor Sites and to Monitor Cancer Response to Hormonal Therapy.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Hinev A; Chaushev B; Klisarova A

**INSTITUCIÓN / INSTITUTION:** - Department of Surgery, Clinic of Urology, Varna Medical University, Varna, Bulgaria.


**TÍTULO / TITLE:** - Hypertension in adolescence is not an independent risk factor for renal cancer: a cohort study of 918,965 males.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Leiba A; Kark JD; Afek A; Derazne E; Keinan-Boker L; Shamiss A; Kreiss Y

**INSTITUCIÓN / INSTITUTION:** - Nephrology and Hypertension Institute, Chaim Sheba Medical Center, Tel Hashomer, Israel; Department of Military Medicine, the Hebrew University, Jerusalem, Israel. Electronic address: aleiba@mah.harvard.edu.

**RESUMEN / SUMMARY:** - BACKGROUND: Hypertension has been repeatedly linked to renal cell cancer, independent of overweight and anti-hypertensive drug use, but its role remains unclear, especially within the growing group of relatively young-middle aged renal cancer patients. In order to delineate the role of hypertension in early onset renal cancer, we examined the association of blood pressure measured at age 17 with the incidence of renal cancer.

**METHODS:** Sociodemographic and medical data of 918,965 adolescent males examined for fitness for military service from 1967 to 2005 were linked to the National Cancer Registry in this nationwide population-based cohort study (12,910,585 person years) to obtain cancer incidence. A single measurement of blood pressure at age 17 was stratified as optimal (<120/80), normal (>=120/80 < 130/85), high normal (>=130/85 < 140/90), or high (>=140/90). We used Cox proportional hazards modeling to estimate the hazard ratio of the blood pressure categories for renal cancer, adjusted for year of birth, body mass index, origin of parents, and height. We also assessed the role of a clinical diagnosis of persistent hypertension (n = 4223, based on multiple measurements).

**RESULTS:** Of those who had their blood pressure recorded, 90 examinees developed renal cancer. In a multivariable model, the higher categories of blood pressure were associated with a decreased risk of renal
cancer (hazard ratio, 0.32; 95% confidence interval, 0.12-0.84; P = .021 for blood pressure \( \geq 140/90 \) vs < 120/80). Furthermore, there was no evidence of increased risk for those with an established diagnosis of hypertension (hazard ratio, 1.28; 95% confidence interval, 0.17-9.50; P = .81). CONCLUSIONS: It is unlikely that hypertension in adolescents carries an increased risk for renal cancer.

[1264]
TÍTULO / TITLE: - Anti-Bladder-Tumor Effect of Baicalein from Scutellaria baicalensis Georgi and Its Application In Vivo.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Evid Based Complement Alternat Med.
●●Enlace al texto completo (gratuito o de pago) 1155/2013/579751
AUTORES / AUTHORS: - Wu JY; Tsai KW; Li YZ; Chang YS; Lai YC; Laio YH; Wu JD; Liu YW
INSTITUCIÓN / INSTITUTION: - Department of Microbiology, Immunology and Biopharmaceuticals, College of Life Sciences, National Chiayi University, No. 300 Syuefu Road, Chiayi 600, Taiwan.
RESUMEN / SUMMARY: - Some phytochemicals with the characteristics of cytotoxicity and/or antimetastasis have generated intense interest among the anticancer studies. In this study, a natural flavonoid baikalein was evaluated in bladder cancer in vitro and in vivo. Baicalein inhibits 5637 cell proliferation. It arrests cells in G1 phase at 100 \( \mu \)M and in S phase below 75 \( \mu \)M. The protein expression of cyclin B1 and cyclin D1 is reduced by baikalein. Baicalein-induced p-ERK plays a minor role in cyclin B1 reduction. Baicalein-inhibited p65NF- kappa B results in reduction of cell growth. Baicalein-induced pGSK(ser9) has a little effect in increasing cyclin B1/D1 expression instead. The translation inhibitor cycloheximide blocks baikalein-reduced cyclin B1, suggesting that the reduction is caused by protein synthesis inhibition. On the other hand, neither cycloheximide nor proteasome inhibitor MG132 completely blocks baikalein-reduced cyclin D1, suggesting that baikalein reduces cyclin D1 through protein synthesis inhibition and proteasomal degradation activation. In addition, baikalein also inhibits cell invasion by inhibiting MMP-2 and MMP-9 mRNA expression and activity. In mouse orthotopic bladder tumor model, baikalein slightly reduces tumor size but with some hepatic toxicity. In summary, these results demonstrate the anti-bladder-tumor properties of the natural compound baikalein which shows a slight anti-bladder-tumor effect in vivo.

[1265]
TÍTULO / TITLE: - Correlation between ICAM1 and VCAM1 gene polymorphisms and histopathological changes in kidney allograft biopsies.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
RESUMEN / SUMMARY: - INTRODUCTION: The immunoglobulin-like molecules intercellular adhesion molecule-1 (ICAM-1) and vascular adhesion molecule-1 (VCAM-1) are responsible for endothelial cell-leukocyte adhesion followed by transmigration of leukocytes through the endothelial cell lining. The aim of this study was to examine the correlation between polymorphisms in ICAM1 and VCAM1 genes and histopathological changes in transplanted kidney biopsies. MATERIAL AND METHODS: The study enrolled 82 Caucasian renal transplant recipients (48 males, 34 females). Genotyping of the rs5498 ICAM1 and the rs1041163 and rs3170794 VCAM1 gene polymorphisms was performed using real-time polymerase chain reaction (PCR). Biopsies were performed in 82 patients and were reviewed by a renal pathologist and the Banff working classification criteria were used. RESULTS: There were no significant associations between VCAM gene polymorphisms and histopathological changes in kidney allograft biopsies. ICAM1 gene polymorphism was associated with the grade of interstitial fibrosis. Interstitial fibrosis was more severe among individuals with the G allele than those with the A allele (AA vs. GG+AG, p = 0.017). There were no statistically significant associations between ICAM1 gene polymorphism and other histopathological changes in kidney allograft biopsies. CONCLUSIONS: The results of our study suggest that rs5498 ICAM1 gene polymorphism is associated with the grade of interstitial fibrosis in kidney recipients and the changes are more severe in patients with the G allele.

TÍTULO / TITLE: - MTHFR C677T polymorphisms are associated with aberrant methylation of the IGF-2 gene in transitional cell carcinoma of the bladder.

RESUMEN / SUMMARY: - The purpose of this study was to determine the relationship between methylation status of the insulin-like growth factor 2 (IGF-
2) gene and methylenetetrahydrofolate reductase (MTHFR) C677T gene polymorphisms in bladder transitional cell carcinoma tissues in a Chinese population. The polymorphisms of the folate metabolism enzyme gene MTHFR were studied by restrictive fragment length polymorphism (RFLP). PCR-based methods of DNA methylation analysis were used to detect the CpG island methylation status of the IGF-2 gene. The association between the methylation status of the IGF-2 gene and clinical characteristics, as well as MTHFR C677T polymorphisms, was analyzed. Aberrant hypomethylation of the IGF-2 gene was found in 68.3% bladder cancer tissues and 12.4% normal bladder tissues, respectively, while hypomethylation was not detected in almost all normal bladder tissues. The hypomethylation rate of the IGF-2 gene in cancer tissues was significantly higher in patients with lymph node metastasis than in those without lymph node metastasis (46.3% vs 17.2%, P = 0.018). No association was found between aberrant DNA methylation and selected factors including sex, age, tobacco smoking, alcohol consumption and green tea consumption. After adjusting for potential confounding variables the variant allele of MTHFR C677T was found to be associated with hypomethylation of the IGF-2 gene. Compared with wildtype CC, the odds ratio was 4.33 (95% CI=1.06-10.59) for CT and 4.95 (95% CI=1.18-12.74) for TT. MTHFR 677 CC and CT genotypes might be one of the reasons that cause abnormal hypomethylation of the IGF-2 gene, and the aberrant CpG island hypomethylation of the IGF-2 gene may contribute to the genesis and progression of bladder transitional cell carcinoma.
patient who developed widespread bone metastases of a previously confined to the prostate gland prostate cancer shortly after starting methotrexate therapy for rheumatoid arthritis and large granular lymphocyte leukemia. We believe an immunosuppressive milieu brought on by the methotrexate use in this case is responsible for the rapid progression of prostate cancer leading to the patient’s demise. To the best of our knowledge, no association has been made to date between the therapy with methotrexate and a fulminant course of a previously indolent prostate cancer. Given its utilization in a variety of benign and malignant conditions and the ageing population, caution is advised with the use of this agent, especially in the presence of an underlying malignancy.

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[1270] TÍTULO / TITLE: - Therapeutic vaccines and immunotherapy in castration-resistant prostate cancer. RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary REVISTA / JOURNAL: - Am Soc Clin Oncol Educ Book. 2013;2013:166-70. doi: E10.1200/EdBook_AM.2013.33.e166. ●●Enlace al texto completo (gratuito o de pago) 1200/EdBook_AM.2013.33.e166 AUTORES / AUTHORS: - Gulley JL; Madan RA; Heery CR INSTITUCIÓN / INSTITUTION: - From the Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD. RESUMEN / SUMMARY: - Results of recent clinical trials have intensified interest in immunotherapy for cancer. Among the most promising candidates for immunotherapy are patients with prostate cancer. Results of therapeutic vaccine clinical trials in this population have suggested statistically significant and clinically meaningful improvements in overall survival, with substantially fewer side effects than with chemotherapy. Of particular interest are sipuleucel-T, the first U.S. Food and Drug Administration-approved therapeutic cancer vaccine, and PSA-TRICOM (PROSTVAC), a therapeutic cancer vaccine in phase III testing. The immune checkpoint inhibitor ipilimumab is also stirring considerable interest, with two phase III trials ongoing in prostate cancer. This
article highlights data emerging from these trials and addresses remaining questions and practical clinical implications of this therapeutic strategy.

[1271]
TÍTULO / TITLE: - Long-Term Response to Sunitinib Therapy for Metastatic Renal Cell Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Molina AM; Jia X; Feldman DR; Hsieh JJ; Ginsberg MS; Velasco S; Patil S; Motzer RJ
INSTITUCION / INSTITUTION: - Genitourinary Oncology Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY; Department of Medicine, Weill Medical College of Cornell University, New York, NY. Electronic address: molinaa@mskcc.org.
RESUMEN / SUMMARY: - BACKGROUND: Sunitinib achieves objective response and prolongs progression-free survival (PFS) in patients with metastatic renal cell carcinoma (RCC). A subset of patients achieves long-term responses. The characteristics of patients who achieved long-term response (defined as patients achieving ongoing complete response [CR] or remaining progression free for > 18 months while receiving sunitinib) are reported. PATIENTS AND METHODS: A database of 186 patients treated with sunitinib alone (n = 89) or in combination (n = 97) in 9 clinical trials was reviewed; all had 1 year or more follow-up from sunitinib start to data cutoff for analysis. Median PFS was 10.8 months (95% CI, 8.3-13.3); median overall survival (OS) was 30.4 months (95% CI, 21.5-36.8 months) for the 186 patients. Thirty-four patients were identified as long-term responders because they either had durable CR or remained progression free while receiving sunitinib for > 18 months. RESULTS: Best response for 34 long-term responders was CR in 3 patients, partial response (PR) in 24 patients, and stable disease in 7 patients. The median duration of sunitinib therapy was 24.9 months (range, 18.1-73.9 months). The median PFS among the long-term responders was 17.4 months (95% CI, 7-29.9 months) at a landmark PFS analysis performed after 18 months from treatment start. Univariate analysis from the 186 patients identified bone metastasis, lung metastasis, and intermediate/poor risk groups as adverse prognostic factors for long-term response. CONCLUSION: Sunitinib achieves long-term response in a subset of patients with metastatic RCC. Lack of bone metastasis or lung metastasis and good MSKCC risk status may predict long-term response.

[1272]
TÍTULO / TITLE: - Ablative therapies for small renal tumours.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

926

AUTORES / AUTHORS: Castro A Jr; Jenkins LC; Salas N; Lorber G; Leveillee RJ

INSTITUCIÓN / INSTITUTION: University of Miami School of Medicine, Department of Urology, 1400 NW 10th Avenue, Suite 509b, Miami, FL 33126, USA.

RESUMEN / SUMMARY: Improvements in imaging technology have resulted in an increase in detection of small renal masses (SRMs). Minimally invasive ablation modalities, including cryoablation, radiofrequency ablation, microwave ablation and irreversible electroporation, are currently being used to treat SRMs in select groups of patients. Cryoablation and radiofrequency ablation have been extensively studied. Presently, cryoablation is gaining popularity because the resulting ice ball can be visualized easily using ultrasonography. Tumour size and location are strong predictors of outcome of radiofrequency ablation. One of the main benefits of microwave ablation is that microwaves can propagate through all types of tissue, including desiccated and charred tissue, as well as water vapour, which might be formed during the ablation. Irreversible electroporation has been shown in animal studies to affect only the cell membrane of undesirable target tissues and to spare adjacent structures; however, clinical studies that depict the efficacy and safety of this treatment modality in humans are still sparse. As more experience is gained in the future, ablation modalities might be utilized in all patients with tumours <4 cm in diameter, rather than just as an alternative treatment for high-risk surgical patients.

[1273]
TÍTULO / TITLE: Targeted therapy in advanced urothelial carcinoma.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Verdoorn BP; Kessler ER; Flaig TW
INSTITUCIÓN / INSTITUTION: Division of Medical Oncology, Department of Medicine, University of Colorado School of Medicine, Denver, Colorado, USA.
RESUMEN / SUMMARY: Urothelial carcinoma (UC) is a common and deadly cancer in the United States. While molecularly targeted therapies have been integrated into the standard-of-care management of other solid tumors in recent years, the use of targeted therapy in UC has lagged behind. Accordingly, the management of advanced disease, along with outcomes, has remained largely unchanged for the past 2 decades. Despite the lack of new agents in the clinic, preclinical and early clinical studies have demonstrated that numerous potentially "targetable" molecular pathways exist, including the epidermal growth factor receptor (EGFR), vascular endothelial growth factor receptor (VEGFR), human epidermal growth factor receptor 2 (HER2/neu), and insulin-like growth
factor 1 receptor (IGF1R) pathways. This review focuses on targeted therapies related to these pathways of interest for the treatment of advanced UC, describing the evidence to support further investigation of these approaches. Notably, the identification and validation of new agents will only occur through accrual to urothelial cancer trials designed to answer these questions, which will require the support of the entire urologic community.

[1274]
TÍTULO / TITLE: - Nonhormone therapy for metastatic castration-resistant prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
- Enlace al texto completo (gratuito o de pago) 1200/EdBook_AM.2013.33.e161
AUTORES / AUTHORS: - Fizazi K
INSTITUCIÓN / INSTITUTION: - From the Department of Cancer Medicine, Institut Gustave Roussy, University of Paris Sud, Villejuif, France.
RESUMEN / SUMMARY: - There is no doubt that more therapeutic progress has been achieved during the last 3 years for patients with metastatic castration-resistant prostate cancer (mCRPC) than during the previous 30 years. During this limited time frame, not only have six compounds (sipuleucel-T, cabazitaxel, denosumab, abiraterone, radium-223, and enzalutamide, listed in chronologic order) yielded positive results in phase III trials, we have also learned that their mechanisms of action are different, making it quite likely that part of their anticancer activity may be incremental. Most of these agents have already been approved. Further progress may well soon complete this recently enlarged armamentarium, with important trials testing new agents derived from existing families of compounds (new endocrine therapies, new immunotherapies, etc.) and exploring the activity of new families of agents (tyrosine kinase inhibitors such as cabozantinib, inhibitors of chaperone proteins like OGX-O11 and OGX-427). The availability of these agents creates a new major challenge for those who conduct clinical research in mCRPC. Will we be able to personalize therapy based on the biology of the individual’s tumor, as we are already doing in other neoplasms?

[1275]
TÍTULO / TITLE: - Identification of New Genes Downregulated in Prostate Cancer and Investigation of Their Effects on Prognosis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
- Enlace al texto completo (gratuito o de pago) 1089/gtmb.2012.0524
AUTORES / AUTHORS: - Varisli L
INSTITUCIÓN / INSTITUTION: - Department of Biology, Art and Science Faculty, Harran University, Osmanbey Campus, Sanliurfa, Turkey.

RESUMEN / SUMMARY: - Prostate cancer is the most common noncutaneous malignant neoplasm in men in the Western countries. It is well established that genetic and epigenetic alterations are common events in prostate cancer, which may lead to aberrant expression of critical genes. Most of the studies are focused on the overexpressed or duplicated genes in prostate cancer. However, it is known that some of the differentially expressed genes in prostate cancer are downregulated. Since the inventory of downregulated genes is incomplete, we performed in silico approaches to reveal the novel prostate cancer downregulated genes. Moreover, we also investigated for a possible link between the expression of the downregulated genes and tumor grade, recurrence, metastasis, or survival status in prostate cancer. Our results showed that the expression of GSTP1 and AOX1 are downregulated in prostate cancer, in concordance with previous reports. Moreover, we showed that TPM2, CLU, and COL4A6 mRNA levels are downregulated in prostate cancer. Further, we found a significant negative correlation between the expression of the above-mentioned genes and the prognosis of prostate cancer.

[1276]

TÍTULO / TITLE: - Non-invasive Imaging of Acute Allograft Rejection after Rat Renal Transplantation Using 18F-FDG PET.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Grabner A; Kentrup D; Schnockel U; Gabriels G; Schroter R; Pavenstadt H; Schober O; Schlatter E; Schafers M; Reuter S

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine D, Experimental Nephrology, University of Munster.

RESUMEN / SUMMARY: - The number of patients with end-stage renal disease, and the number of kidney allograft recipients continuously increases. Episodes of acute cellular allograft rejection (AR) are a negative prognostic factor for long-term allograft survival, and its timely diagnosis is crucial for allograft function (1). At present, AR can only be definitely diagnosed by core-needle biopsy, which, as an invasive method, bares significant risk of graft injury or even loss. Moreover, biopsies are not feasible in patients taking anticoagulant drugs and the limited sampling site of this technique may result in false negative results if the AR is focal or patchy. As a consequence, this gave rise to an ongoing search for new AR detection methods, which often has to be done in animals including the use of various transplantation models. Since the early 60s rat renal transplantation is a well-established experimental method for the examination and analysis of AR (2). We herein present in addition small animal positron emission tomography (PET) using (18)F-fluorodeoxyglucose (FDG) to
assess AR in an allogeneic uninephrectomized rat renal transplantation model and propose graft FDG-PET imaging as a new option for a non-invasive, specific and early diagnosis of AR also for the human situation (3). Further, this method can be applied for follow-up to improve monitoring of transplant rejection (4).
considered for this analysis (41%). Some important differences were shown in prescribing and delivering RT, particularly with regards to treatment volumes and fractionation. CONCLUSIONS: Despite the results of clinical trials, several differences still exist among Italian radiation oncologists in the treatment of prostate cancer patients. These patients probably deserve a more uniform approach, based on up-to-date, detailed, and evidence-based recommendations.

[1278]

**TÍTULO / TITLE:** - Blood level omega-3 Fatty acids as risk determinant molecular biomarker for prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Sorongon-Legaspi MK; Chua M; Sio MC; Morales M Jr

**INSTITUCIÓN / INSTITUTION:** - Department of Preventive and Community Medicine, St. Luke’s College of Medicine, Sta. Ignaciana Street, 1102 Quezon City, Philippines.

**RESUMEN / SUMMARY:** - Previous researches involving dietary methods have shown conflicting findings. Authors sought to assess the association of prostate cancer risk with blood levels of omega-3 polyunsaturated fatty acids (n-3 PUFA) through a meta-analysis of human epidemiological studies in available online databases (July, 2012). After critical appraisal by two independent reviewers, Newcastle-Ottawa Quality Assessment Scale (NOQAS) was used to grade the studies. Six case control and six nested case control studies were included. Results showed nonsignificant association of overall effect estimates with total or advanced prostate cancer or high-grade tumor. High blood level of alpha-linolenic acid (ALA) had nonsignificant positive association with total prostate cancer risk. High blood level of docosapentaenoic acid (DPA) had significant negative association with total prostate cancer risk. Specific n-3 PUFA in fish oil, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) had positive association with high-grade prostate tumor risk only after adjustment of interstudy variability. There is evidence that high blood level of DPA that is linked with reduced total prostate cancer risk and elevated blood levels of fish oils, EPA, and DHA is associated with high-grade prostate tumor, but careful interpretation is needed due to intricate details involved in prostate carcinogenesis and N-3 PUFA metabolism.

[1279]

**TÍTULO / TITLE:** - Effect of bladder distension on dosimetry of organs at risk in computer tomography based planning of high-dose-rate intracavitary brachytherapy for cervical cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Patra NB; Manir KS; Basu S; Goswami J; Kabasi AK; Sarkar SK

INSTITUCIÓN / INSTITUTION: - Radiotherapy Department, Medical College and Hospitals, Kolkata, India.

RESUMEN / SUMMARY: - PURPOSE: Distension and shape of urinary bladder may vary during intracavitary brachytherapy (ICBT) for cervical cancer, significantly affecting doses to bladder, rectum, sigmoid colon and small intestine and consequently late radiation toxicities. This study is to evaluate the effects of different fixed volume bladder distention on dosimetry, assessed by three dimensional image based planning, in different organs at risk during the treatment of cervical cancer with ICBT. MATERIAL AND METHODS: Forty seven cervical cancer patients (stage IB to IVA) were qualified for ICBT following external beam radiotherapy. Urinary bladder was distended with different volumes of normal saline instilled by a Foley’s catheter. Planning CT scans were performed after insertion of applicators and three dimensional treatment planning was done on Brachyvision® treatment planning system (Varian Medical Systems, Palo Alto, CA). Dose volume histograms were analyzed. Bladder, rectum, sigmoid colon and small intestine doses were collected for individual plans and compared, based on the amount of bladder filling. RESULTS: Mean dose to the bladder significantly decreased with increased bladder filling. However, doses to the small volumes (0.1 cc, 1 cc, 2 cc) which are relevant for brachytherapy, did not change significantly with bladder filling for bladder, rectum or sigmoid colon. Nevertheless, all dose values of small intestine are decreased significantly with bladder filling. CONCLUSIONS: Bladder distension has no significant effect on doses received during brachytherapy by relevant volumes of bladder, rectum and sigmoid colon except intestine where values are decreased with bladder distension. A larger study with clinical correlation of late toxicities is essential for proper evaluation of this strategy.

TÍTULO / TITLE: - Non-invasive magnetic resonance imaging in rats for prediction of the fate of grafted kidneys from cardiac death donors.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


[1280]
The main objective of this study was to assess cardiac death (CD) kidney grafts before transplantation to determine whether blood oxygen level-dependent (BOLD) and diffusion MRI techniques can predict damage to these grafts after transplantation. We assessed CD kidney tissue by BOLD and diffusion MRI. We also examined pathological and gene expression changes in CD kidney grafts before and after transplantation. Although there was significantly more red cell congestion (RCC) in the inner stripe of the outer medulla (IS) in both 1 h after cardiac death (CD1h) and CD2h kidneys destined for grafts before transplantation compared with CD0h (p<0.05), CD2h, but not CD1h, kidney grafts had significantly different RCC in the IS 2 days after transplantation (p<0.05). Consistent with these pathological findings, tissue plasminogen activator (tPA) gene expression was increased only in the cortex and medulla of CD2h kidney grafts after transplantation. BOLD MRI successfully and non-invasively imaged and quantified RCC in the IS in both CD1h and CD2h kidney grafts (p<0.05). Diffusion MRI also non-invasively assessed increased the apparent diffusion coefficient in the IS and decreased it in the outer stripe (OS) of CD2h grafts, in concordance with interstitial edema in the IS and tubule cellular edema in the OS. These two types of edema in the outer medulla could explain the prolonged RCC in the IS only of CD2h kidney grafts, creating part of a vicious cycle inhibiting red cells coming out of capillary vessels in the IS. Perfusion with University of Wisconsin solution before MRI measurements did not diminish the difference in tissue damage between CD1h and CD2h kidney grafts. BOLD and diffusion MRI, which are readily available non-invasive tools for evaluating CD kidney grafts tissue damage, can predict prolonged organ damage, and therefore the outcome, of transplanted CD kidney grafts.
PURPOSE: To evaluate the prevalence of bladder neck contracture (BNC) and its risk factors in patients undergoing radical prostatectomy in Korea.

MATERIALS AND METHODS: We analyzed data from 488 patients with prostatic cancer who underwent radical prostatectomy performed by seven surgeons in seven hospitals, including 365 open radical prostatectomies (ORPs), 99 laparoscopic radical prostatectomies (LRPs), and 24 robot-assisted laparoscopic radical prostatectomies (RARPs). Patients with BNCs were compared with those without BNCs to identify the risk factors for BNC occurrence.

RESULTS: Overall, BNCs occurred in 21 of 488 patients (4.3%): 17 patients (4.7%) who underwent ORP, 4 patients (4%) who underwent LRP, and no patients who underwent RARP. In the univariate analysis, men with BNCs had a longer length of time before drain removal (12 days vs. 6.8 days, p<0.001), which reflected urinary leakage through the vesicourethral anastomosis. In the multivariate analysis, the length of time before drain removal was the only predictor of BNC (odds ratio, 1.12; p=0.001). Intraoperative blood loss was higher in patients with BNC, but the difference was not statistically significant.

CONCLUSIONS: The most significant factor related to BNC occurrence after radical prostatectomy in our study was the length of time before drain removal, which reflects urinary leakage from the vesicourethral anastomosis. The proper formation of a watertight anastomosis to decrease urinary leakage may help to reduce the occurrence of BNC.
RESUMEN / SUMMARY: For nearly three decades, gonadotropin-releasing hormone (GnRH) agonists, particularly leuprorelin acetate (LA), have served as an important part of the treatment armamentarium for prostate cancer. The introduction of LA depot formulations provided a significant improvement in the acceptance of this therapy; however, their indicated treatment duration of 1 to 4 months was still not long enough to satisfy all medical needs. For this reason some manufacturers developed new injectable formulations that provide testosterone suppression for 6 months. This review article assesses key publications in order to compare these long-acting, commercially available, LA depot formulations and their clinical performance. The literature search identified 14 publications; by excluding reviews, duplications, and non-English articles, only three original papers describing clinical trial remained for review: two focused on microsphere-based LA formulations with either a 30 mg or 45 mg dose and one focused on a gel-based leuprorelin acetate with a 45 mg dose. All products were tested in individual clinical trials and have demonstrated their efficacy and safety.

TÍTULO / TITLE: Evaluation of Argonaute protein as a predictive marker for human clear cell renal cell carcinoma.

RESUMEN / SUMMARY: Argonaute subfamily proteins are involved in human organ growth and development. Recent studies found its association with human breast cancer, however, its expression profile and its prognostic value in clear cell renal cancer (ccRCC) have not been investigated. METHODS: Expression of the Argonaute proteins were assessed by immunohistochemistry (IHC) in tissue microarrays (TMA), containing paired tumor tissue and adjacent non-cancer tissue from 176 patients who had undergone surgery in hospital for histologically proven ccRCC. Prognostic value and correlation with other clinicopathologic factors were evaluated in two classifications. RESULTS: Data
showed a significant higher expression of Argonaute 1 and Argonaute 2 present in neoplastic tissues compared with that in adjacent tissue; A significant correlation existed between the higher expression of Argonaute 1 protein with the T stage, lymph node metastasis and clinical TNM (cTNM); Survival analysis by Kaplan-Meier survival curve and log-rank test demonstrated that elevated Argonaute 1 and Argonaute 2 expression in cancer tissue predicted poorer overall survival (OS) compared with group in lower expression (36.3% VS 67.1%; 37.3% VS 53.9%; respectively). Notably, multivariate analyses by Cox’s proportional hazard model revealed that expression of Argonaute 2 was an independent prognostic factor in renal cancer. CONCLUSIONS: In summary, our present study clarify that the aberrant expression of Argonaute in human RCC is possibly involved with tumorigenesis and development, and the Argonaute protein could act as a potential biomarker for prognosis assessment of renal cancer. Related mechanism is worthy of further investigation.

[1285]
TITULO / TITLE: - Prostate cancer: Risk versus benefit of lymph node dissection during prostatectomy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kane CJ; Liss MA
INSTITUCIÓN / INSTITUTION: - Department of Urology, UC San Diego Health System, San Diego, CA 92013, USA.

[1286]
TITULO / TITLE: - Evaluating the expression of oct4 as a prognostic tumor marker in bladder cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hatefi N; Nouraei N; Parvin M; Ziaee SA; Mowla SJ
INSTITUCIÓN / INSTITUTION: - Department of Molecular Genetics, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran ; Department of Pathology, Labbafi-Nejad Medical Centre, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
RESUMEN / SUMMARY: - OBJECTIVES: The key transcriptional regulator Oct4 is one of the self-renewal and differentiation-related factors in cancer stem cells, where it maintains “stemness” state. Cancer stem cells have been identified in a variety of solid malignancies. They are a small population of tumor cells with stem cell characteristics, which are a likely cause of relapse in cancer patients. Due to high incidence, mortality, and recurrence rates of bladder cancer and the necessity of accurate prediction of malignant behavior of the tumors, we
evaluated the prognostic value of Oct4 expression in formalin-fixed paraffin-embedded (FFPE) tissues of bladder cancer. MATERIALS AND METHODS: In this study, Oct4 expression was evaluated in 52 (FFPE) tissues of bladder cancer. RNA extraction from samples of 30 patients from the archive of Labbafi-Nejad Medical Centre in Tehran was performed and Oct4 expression levels were examined by semi-quantitative RT-PCR. The intracellular distribution of Oct4 protein was also determined by immunohistochemistry (IHC). RESULTS: The results revealed a significant correlation between the expression level of Oct4 and the tumors’ grade and stage. A mostly cytoplasmic distribution of Oct4 protein was also confirmed by IHC. CONCLUSION: All together, our data indicate that the expression level of Oct4 gene is correlated with the clinical and histopathological prognostic indexes of tumors and thus can be considered as a potential prognostic tumor marker.

[1287]
TITULO / TITLE: - ERG induces epigenetic activation of Tudor domain-containing protein 1 (TDRD1) in ERG rearrangement-positive prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kacprzyk LA; Laible M; Andrasiuk T; Brase JC; Borno ST; Falth M; Kuner R; Lehrach H; Schweiger MR; Sultmann H
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kacprzyk@ugabiopharma.com
RESUMEN / SUMMARY: - BACKGROUND: Overexpression of ERG transcription factor due to genomic ERG-rearrangements defines a separate molecular subtype of prostate tumors. One of the consequences of ERG accumulation is modulation of the cell’s gene expression profile. Tudor domain-containing protein 1 gene (TDRD1) was reported to be differentially expressed between TMPRSS2:ERG-negative and TMPRSS2:ERG-positive prostate cancer. The aim of our study was to provide a mechanistic explanation for the transcriptional activation of TDRD1 in ERG rearrangement-positive prostate tumors. METHODOLOGY / PRINCIPAL FINDINGS: Gene expression measurements by real-time quantitative PCR revealed a remarkable co-expression of TDRD1 and ERG (r(2) = 0.77) but not ETV1 (r(2)<0.01) in human prostate cancer in vivo. DNA methylation analysis by MeDIP-Seq and bisulfite sequencing showed that TDRD1 expression is inversely correlated with DNA methylation at the TDRD1 promoter in vitro and in vivo (rho = -0.57). Accordingly, demethylation of the TDRD1 promoter in TMPRSS2:ERG-negative prostate cancer cells by DNA
methyltransferase inhibitors resulted in TDRD1 induction. By manipulation of ERG dosage through gene silencing and forced expression we show that ERG governs loss of DNA methylation at the TDRD1 promoter-associated CpG island, leading to TDRD1 overexpression. CONCLUSIONSSIGNIFICANCE: We demonstrate that ERG is capable of disrupting a tissue-specific DNA methylation pattern at the TDRD1 promoter. As a result, TDRD1 becomes transcriptionally activated in TMPRSS2:ERG-positive prostate cancer. Given the prevalence of ERG fusions, TDRD1 overexpression is a common alteration in human prostate cancer which may be exploited for diagnostic or therapeutic procedures.

[1288]

TÍTULO / TITLE: - Consumption of Fish Products across the Lifespan and Prostate Cancer Risk.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Torfadottir JE; Valdimarsdottir UA; Mucci LA; Kasperzyk JL; Fall K; Tryggvadottir L; Aspelund T; Olafsson O; Harris TB; Jonsson E; Tulinius H; Gudnason V; Adami HO; Stampfer M; Steingrimsdottir L

INSTITUCIÓN / INSTITUTION: - Centre of Public Health Sciences, University of Iceland, Reykjavik, Iceland ; Educational Research Institute, School of Education, University of Iceland, Reykjavik, Iceland.

RESUMEN / SUMMARY: - OBJECTIVE: To examine whether fish and fish oil consumption across the lifespan is associated with a lower risk of prostate cancer. DESIGN: The study was nested among 2268 men aged 67-96 years in the AGES-Reykjavik cohort study. In 2002 to 2006, dietary habits were assessed, for early life, midlife and later life using a validated food frequency questionnaire. Participants were followed for prostate cancer diagnosis and mortality through 2009 via linkage to nationwide cancer- and mortality registers. Adjusting for potential confounders, we used regression models to estimate odds ratios (ORs) and hazard ratios (HRs) for prostate cancer according to fish and fish oil consumption. RESULTS: Among the 2268 men, we ascertained 214 prevalent and 133 incident prostate cancer cases, of which 63 had advanced disease. High fish consumption in early- and midlife was not associated with overall or advanced prostate cancer. High intake of salted or smoked fish was associated with a 2-fold increased risk of advanced prostate cancer both in early life (95% CI: 1.08, 3.62) and in later life (95% CI: 1.04, 5.00). Men consuming fish oil in later life had a lower risk of advanced prostate cancer [HR (95%CI): 0.43 (0.19, 0.95)], no association was found for early life or midlife consumption. CONCLUSIONS: Salted or smoked fish may increase risk of...
advanced prostate cancer, whereas fish oil consumption may be protective against progression of prostate cancer in elderly men. In a setting with very high fish consumption, no association was found between overall fish consumption in early or midlife and prostate cancer risk.
BACKGROUND: Prostate cancer is a known cause of mortality in men worldwide although the risk factor varies among different ethnic groups. Loss of the Y chromosome is a common chromosomal abnormality observed in the human prostate cancer. RESULTS: We screened 51 standard sequence tagged sites (STSs) corresponding to a male-specific region of the Y chromosome (MSY), sequenced the coding region of the SRY gene and assessed the status of the DYZ1 arrays in the human prostate cancer cell lines DU145 and LNCaP. The MSY was found to be intact and coding region of SRY showed no sequence variation in both the cell lines. However, DYZ1 arrays showed sequence and copy number variations. DU145 and LNCaP cells were found to carry 742 and 1945 copies of the DYZ1, respectively per 3.3 pg of genomic DNA. The DYZ1 copies detected in these cell lines are much below the average of that reported in normal human males. Similarly, the number of “TTCCA” repeat and its derivatives within the DYZ1 arrays showed variation compared to those of the normal males. CONCLUSIONS: Clearly, the DYZ1 is maximally affected in both the cell lines. Work on additional cell lines and biopsied samples would augment our understanding about the susceptibility of this region. Based on the present work, we construe that copy number status of the DYZ1 may be exploited as a supplementary prognostic tool to monitor the occurrence of prostate cancer using biopsied samples.

Neuroendocrine (NE) differentiation has gained increased attention as a prostate cancer (PC) prognostic marker. The aim of this study is to determine whether host germline genetic variation influences tumor progression and metastasis in C57BL/6-Tg(TRAMP)8247Ng/J (TRAMP)
mouse model of aggressive NEPC. TRAMP mice were crossed to the eight progenitor strains of the Collaborative Cross recombinant inbred panel to address this. Tumor growth and metastasis burden were quantified in heterozygous transgene positive F1 male mice at 30 weeks of age. Compared to wild-type C57BL/6J-Tg(TRAMP)824Ng/J males, TRAMP x CAST/EiJ, TRAMP x NOD/ShiLtJ and TRAMP x NZO/HILtJ F1 males displayed significant increases in tumor growth. Conversely, TRAMP x WSB/EiJ and TRAMP x PWK/PhJ F1 males displayed significant reductions in tumor growth. Interestingly, despite reduced tumor burden, TRAMP x WSB/EiJ males had an increased nodal metastasis burden. Patterns of distant pulmonary metastasis tended to follow the same patterns as that of local dissemination in each of the strains. All tumors and metastases displayed positive staining for NE markers, synaptophysin, and FOXA2. These experiments conclusively demonstrate that the introduction of germline variation by breeding modulates tumor growth, local metastasis burden, and distant metastasis frequency in this model of NEPC. These strains will be useful as model systems to facilitate the identification of germline modifier genes that promote the development of aggressive forms of PC.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

[1293] TITULO / TITLE: - Serum leptin and adiponectin levels and risk of renal cell carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
OBJECTIVE: The incidence of renal cell carcinoma (RCC) has increased rapidly in the U.S., particularly among African Americans. Despite a well-established link between obesity and RCC, the mechanism through which obesity increases cancer risk has yet to be established. Adipokines, such as leptin and adiponectin, may link obesity and cancer, with different quantitative effects by race. DESIGN AND METHODS: We evaluated the association between leptin and adiponectin concentrations and RCC risk among Caucasians (581 cases, 558 controls) and African Americans (187 cases, 359 controls) in a case-control study conducted in Detroit and Chicago. Odds ratios (ORs) and 95% confidence intervals (95%CIs) were estimated using unconditional logistic regression. RESULTS: Among controls, Caucasians had higher median adiponectin than African Americans (males: 8.2 vs. 7.0 mug/ml, P = 0.001; females: 13.4 vs. 8.4 mug/ml, P < 0.0001), and lower median leptin than African Americans (males: 11.8 vs. 14.1 ng/ml, P = 0.04; females: 28.3 vs. 45.9 ng/ml, P < 0.0001). Among Caucasians, the ORs for RCC comparing the highest (Q4) to the lowest (Q1) sex-specific quartile of leptin were 3.2 (95% CI: 1.9-5.2) for males and 4.7 (95% CI: 2.6-8.6) for females. Serum leptin was not significantly associated with RCC among African American males (OR 1.5, 95% CI: 0.7-3.1) or females (OR 2.1, 95% CI: 0.8-5.5). Higher adiponectin was associated with RCC risk among African American males (Q4 vs. Q1: OR 2.3, 95% CI: 1.1-4.6) and females (OR 2.1, 95% CI: 1.2-6.7), but not significantly among Caucasian males (OR 1.6, 95% CI: 0.99-2.7) and females (OR 1.6, 95% CI: 0.9-3.1). CONCLUSION: We observed an association between both leptin and adiponectin concentrations and risk of RCC, which may differ by race. Confirmation in further investigations is needed.
AUTHORS / AUTHORS: - Freedland SJ; Hamilton RJ; Gerber L; Banez LL; Moreira DM; Andriole GL; Rittmaster RS

INSTITUTION / INSTITUTION: - 1] Surgery Section, Durham VA Medical Center, Durham, NC, USA [2] Duke Prostate Center, Division of Urological Surgery, Department of Surgery, Duke University School of Medicine, Durham, NC, USA [3] Department of Pathology, Duke University School of Medicine, Durham, NC, USA.

RESUMEN / SUMMARY: - Background: Statins are associated with lower PSA levels. As PSA is the primary method for prostate cancer (PC) screening, this confounds any associations between statins and risk of being diagnosed with PC. Thus, we examined the association between statins and cancer and high-grade cancer in REDUCE, where biopsies were largely PSA-independent. Methods: Post-hoc secondary analysis of REDUCE, which was a prospective multinational randomized controlled trial of dutasteride vs placebo for 4 years among men aged 50-75 years with PSA of 2.5-10.0 ng ml-1 and a negative biopsy at baseline, and included PSA-independent biopsies mandated at 2- and 4-years. Analyses were limited to men who underwent at least one biopsy while under study (n=6729). The association between baseline statin use and risk of overall, high-grade (Gleason >/=7) or low-grade (Gleason </=6) PC vs no cancer was examined using multinomial logistic regression adjusting for age, race, baseline PSA, prostate volume, rectal examination findings, body mass index (BMI), comorbidities, smoking, alcohol intake and treatment arm. Results: Of 6729 men who had at least one biopsy while on study, 1174 (17.5%) were taking a statin at baseline. Men taking statins were older, had lower PSA levels, higher BMI values and lower serum testosterone and dihydrotestosterone levels, though differences, were slight. Statin use was not associated with overall PC diagnosis (multivariable OR 1.05, 95% CI 0.89-1.24, P=0.54). When stratified by grade, statin use was not associated with low-grade (multivariable OR 1.03, 95% CI 0.85-1.25, P=0.75) or high-grade cancer (multivariable OR 1.11, 95% CI 0.85-1.45, P=0.46). The major limitation is the inclusion of only men with a negative baseline biopsy. Conclusions: Among men with a negative baseline biopsy and follow-up biopsies largely independent of PSA, statins were not associated with cancer or high-grade cancer. Prostate Cancer and Prostatic Disease advance online publication, 9 April 2013; doi:10.1038/pcan.2013.10.

[1296] TÍTULO / TITLE: - Rosiglitazone is not associated with an increased risk of bladder cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

RESUMEN / SUMMARY: - BACKGROUND: Whether rosiglitazone may increase bladder cancer risk has not been extensively investigated. METHODS: The reimbursement databases of all Taiwanese diabetic patients under oral anti-diabetic agents or insulin from 1996 to 2009 were retrieved from the National Health Insurance. An entry date was set at 1 January 2006 and a total of 885,236 patients with type 2 diabetes were followed up for bladder cancer incidence till end of 2009. Incidences for ever-users, never-users and subgroups of rosiglitazone exposure (using tertile cutoffs of time since starting rosiglitazone, duration of therapy and cumulative dose) were calculated and hazard ratios estimated by Cox regression. RESULTS: There were 102,926 ever-users and 782,310 never-users, respective numbers of incident bladder cancer 356 (0.35%) and 2753 (0.35%), and respective incidence 98.3 and 101.6 per 100,000 person-years. The overall hazard ratios (95% confidence intervals) did not show significant association in unadjusted model [0.969 (0.867, 1.082)] and models adjusted for age and sex [0.983 (0.880, 1.098)] or all covariates [0.980 (0.870, 1.104)]. Neither the P values for the hazard ratios for the different categories of the dose-responsive parameters, nor their P-trends were significant. CONCLUSIONS: Rosiglitazone does not increase the risk of bladder cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
RESUMEN / SUMMARY: - Wilms’ tumor (WT) is the most common abdominal tumor in children. Many pediatric renal tumors in the past were categorized as WT; however, in recent years, several specific renal tumors have been recognized as distinct pathological entities. The age and clinical presentation of the child and distinctive imaging features may help in reaching a specific diagnosis in most cases. This is important as it has implications on the pre-operative diagnostic work-up and prognosis of the child. However, it is often not possible to differentiate one from the other pediatric renal tumor on the basis of imaging alone, and the final diagnosis is often made at histological examination of the surgical specimen. This article reviews the imaging features of primary malignant renal neoplasms in children along with their clinical presentation and pathological features.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Anand R; Narula MK; Gupta I; Chaudhary V; Choudhury SR; Jain M
INSTITUCIÓN / INSTITUTION: - Department of Radiodiagnosis, Lady Hardinge Medical College and Associated Smt. Sucheta Kriplani and Kalawati Hospitals, New Delhi, India.

AUTORES / AUTHORS: - Dobrynin P; Matyunina E; Malov SV; Kozlov AP
INSTITUCIÓN / INSTITUTION: - The Biomedical Center, Saint Petersburg 194044, Russia ; Dobzhansky Center for Genome Bioinformatics, Saint Petersburg State University, Saint Petersburg 190004, Russia.
RESUMEN / SUMMARY: - In order to be inherited in progeny generations, novel genes should originate in germ cells. Here, we suggest that the testes may play a special "catalyst" role in the birth and evolution of new genes. Cancer/testis antigen encoding genes (CT genes) are predominantly expressed both in testes and in a variety of tumors. By the criteria of evolutionary novelty, the CT genes are, indeed, novel genes. We performed homology searches for sequences similar to human CT in various animals and established that most of the CT genes are either found in humans only or are relatively recent in their origin. A majority of all human CT genes originated during or after the origin of Eutheria. These results suggest relatively recent origin of human CT genes and align with the hypothesis of the special role of the testes in the evolution of the gene families.

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TÍTULO / TITLE: - Five-year downstream outcomes following prostate-specific antigen screening in older men.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - JAMA. Acceso gratuito al texto completo.

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● Enlace al texto completo (gratuito o de pago) 1001/jamainternmed.2013.323

AUTORES / AUTHORS: - Walter LC; Fung KZ; Kirby KA; Shi Y; Espaldon R; O'Brien S; Freedland SJ; Powell AA; Hoffman RM

RESUMEN / SUMMARY: - IMPORTANCE Despite ongoing controversies surrounding prostate-specific antigen (PSA) screening, many men 65 years or older undergo screening. However, few data exist that quantify the chain of events following screening in clinical practice to better inform decisions.

OBJECTIVE To quantify 5-year downstream outcomes following a PSA screening result exceeding 4.0 ng/mL in older men.

DESIGN AND SETTING Longitudinal cohort study in the national Veterans Affairs health care system.

PARTICIPANTS In total, 295,645 men 65 years or older who underwent PSA screening in the Veterans Affairs health care system in 2003 and were followed up for 5 years using national Veterans Affairs and Medicare data.

MAIN OUTCOME MEASURES Among men whose index screening PSA level exceeded 4.0 ng/mL, we determined the number who underwent prostate biopsy, were diagnosed as having prostate cancer, were treated for prostate cancer, and were treated for prostate cancer and were alive at 5 years according to baseline characteristics. Biopsy and treatment complications were also assessed.

RESULTS In total, 25,208 men (8.5%) had an index PSA level exceeding 4.0 ng/mL. During the 5-year follow-up period, 8,313 men (33.0%) underwent at least 1 prostate biopsy, and 5,220 men (62.8%) who underwent prostate biopsy were diagnosed as having prostate cancer, of whom 4,284 (82.1%) were treated for prostate cancer. Performance of prostate biopsy decreased with advancing age and worsening comorbidity (P < .001), whereas the percentage treated for biopsy-detected cancer exceeded 75% even among men 85 years or older, those with a Charlson-Deyo Comorbidity Index of 3 or higher, and those having low-risk cancer. Among men with biopsy-detected cancer, the risk of death from non-prostate cancer causes increased with advancing age and worsening comorbidity (P < .001). In total, 468 men (5.6%) had complications within 7 days after prostate biopsy. Complications of prostate cancer treatment included new urinary incontinence in 584 men (13.6%) and new erectile dysfunction 588 men (13.7%).

CONCLUSIONS AND RELEVANCE Performance of prostate biopsy is uncommon in older men with abnormal screening PSA levels and decreases with advancing age and...
worsening comorbidity. However, once cancer is detected on biopsy, most men undergo immediate treatment regardless of advancing age, worsening comorbidity, or low-risk cancer. Understanding downstream outcomes in clinical practice should better inform individualized decisions among older men considering PSA screening.

[1301]
TÍTULO / TITLE: Bladder cancer epidemiology and genetic susceptibility.
RESEÑA / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Chu H; Wang M; Zhang Z
INSTITUCIÓN / INSTITUTION: Department of Environmental Genomics, Jiangsu Key Laboratory of Cancer Biomarkers, Prevention and Treatment, Cancer Center, Nanjing Medical University, Nanjing, Jiangsu 211166, China; Department of Genetic Toxicology, the Key Laboratory of Modern Toxicology of Ministry of Education, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu 211166, China.
RESEÑA / SUMMARY: Bladder cancer is the most common malignancy of the urinary system. The incidence of bladder cancer of men is higher than that of women (approximately 4:1). Here, we summarize the bladder cancer-related risk factors, including environmental and genetic factors. In recent years, although the mortality rate induced by bladder cancer has been stable or decreased gradually, the public health effect may be pronounced. The well-established risk factors for bladder cancer are cigarette smoking and occupational exposure. Genetic factors also play important roles in the susceptibility to bladder cancer. A recent study demonstrated that hereditary non-polyposis colorectal cancer is associated with increased risk of bladder cancer. Since 2008, genome-wide association study (GWAS) has been used to identify the susceptibility loci for bladder cancer. Further gene-gene or gene-environment interaction studies need to be conducted to provide more information for the etiology of bladder cancer.

[1302]
TÍTULO / TITLE: Utilization of cone beam CT for reconstruction of dose distribution delivered in image-guided radiotherapy of prostate carcinoma - bony landmark setup compared to fiducial markers setup.
RESEÑA / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Paluska P; Hanus J; Sefrova J; Rouskova L; Grepl J; Jansa J; Kasaova L; Hodek M; Zouhar M; Vosmik M; Petera J
The purpose of this study was to compare two different styles of prostate IGRT: bony landmark (BL) setup vs. fiducial markers (FM) setup. Twenty-nine prostate patients were treated with daily BL setup and 30 patients with daily FM setup. Delivered dose distribution was reconstructed on cone-beam CT (CBCT) acquired once a week immediately after the alignment. Target dose coverage was evaluated by the proportion of the CTV encompassed by the 95% isodose. Original plans employed 1 cm safety margin. Alternative plans assuming smaller 7 mm margin between CTV and PTV were evaluated in the same way. Rectal and bladder volumes were compared with initial ones. While the margin reduction in case of BL setup makes the prostate coverage significantly worse ($p = 0.0003$, McNemar’s test), in case of FM setup with the reduced 7 mm margin, the prostate coverage is even better compared to BL setup with 10 mm margin ($p = 0.049$, Fisher’s exact test). Moreover, partial volumes of organs at risk irradiated with a specific dose can be significantly lowered ($p < 0.0001$, unpaired t-test). Reducing of safety margin is not acceptable in case of BL setup, while the margin can be lowered from 10 mm to 7 mm in case of FM setup.

[1303]

TÍTULO / TITLE: - A new method of establishing orthotopic bladder transplantable tumor in mice.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Yang XH; Ren LS; Wang GP; Zhao LL; Zhang H; Mi ZG; Bai X

INSTITUCIÓN / INSTITUTION: - Department of Comparative Medicine, Shanxi Cancer Institute, Taiyuan 030013, China.

RESUMEN / SUMMARY: - OBJECTIVE: The present study aims to find a convenient, rapid, and stable method to establish bladder tumor in mice. METHODS: Female Balb/C-nu-nu nude mice (or female T739 mice) were narcotized by sodium pentobarbital at a dosage of 60 mg/kg. The stylet of the 24# venous retention needles was bent in a 5 degrees to 7 degrees angle at a distance of 15 mm from the needlepoint to form a circle with 2.61 mm to 3.66 mm radius when the stylet is rotated. The pipe casing was lubricated with liquid paraffin, and inserted into the bladder cavity. The drift angle stylet was inserted into the pipe casing slowly, rotated for five times, and then pulled out. A cell suspension (0.1 mL) of approximately $1 \times 10^6$ T24 cells (or BTT cells) was then injected immediately. RESULTS: A total of 60 T739 mice and 60 Balb/C-nu-nu
nude mice were inoculated with BTT cells and T24 cells, respectively. The bladder tumor incidence and the average survival time of the tumor-bearing mice were 100% and (26.69+/−9.24) d and 100% and (34.59+/−9.8) d for the T739 mice and Balb/C-nu-nu nude mice, respectively. CONCLUSIONS: Using the drift angle stylet to injure the mucous membrane of the urinary bladder can establish a stable bladder transplantable tumor model in mice.

[1304]
TÍTULO / TITLE: - Liver x receptors protect from development of prostatic intraepithelial neoplasia in mice.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago)
1371/journal.pgen.1003483
AUTORES / AUTHORS: - Pommier AJ; Dufour J; Alves G; Viennois E; De Boussac H; Trousson A; Volle DH; Caira F; Val P; Arnaud P; Lobaccaro JM; Baron S
INSTITUCIÓN / INSTITUTION: - Clermont Universite, Universite Blaise Pascal, Genetique Reproduction et Developpement, BP 10448, Clermont-Ferrand, France ; CNRS, UMR 6293, GReD, Aubiere, France ; INSERM, UMR 1103, GReD, Aubiere, France ; Centre de Recherche en Nutrition Humaine d’Auvergne, Clermont-Ferrand, France.
RESUMEN / SUMMARY: - LXR (Liver X Receptors) act as “sensor” proteins that regulate cholesterol uptake, storage, and efflux. LXR signaling is known to influence proliferation of different cell types including human prostatic carcinoma (PCa) cell lines. This study shows that deletion of LXR in mouse fed a high-cholesterol diet recapitulates initial steps of PCa development. Elevation of circulating cholesterol in Lxarapheta/-/- double knockout mice results in aberrant cholesterol ester accumulation and prostatic intra-epithelial neoplasia. This phenotype is linked to increased expression of the histone methyl transferase EZH2 (Enhancer of Zeste Homolog 2), which results in the down-regulation of the tumor suppressors Msmb and Nkx3.1 through increased methylation of lysine 27 of histone H3 (H3K27) on their promoter regions. Altogether, our data provide a novel link between LXR, cholesterol homeostasis, and epigenetic control of tumor suppressor gene expression.

[1305]
TÍTULO / TITLE: - Conditional Transgenic Expression of PIM1 Kinase in Prostate Induces Inflammation-Dependent Neoplasia.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
The Pim proteins are a family of highly homologous protein serine/threonine kinases that have been found to be overexpressed in cancer. Elevated levels of Pim1 kinase were first discovered in human leukemia and lymphomas. However, more recently Pim1 was found to be increased in solid tumors, including pancreatic and prostate cancers, and has been proposed as a prognostic marker. Although the Pim kinases have been identified as oncogenes in transgenic models, they have weak transforming abilities on their own. However, they have been shown to greatly enhance the ability of other genes or chemical carcinogens to induce tumors. To explore the role of Pim1 in prostate cancer, we generated conditional Pim1 transgenic mice, expressed Pim1 in prostate epithelium, and analyzed the contribution of PIM1 to neoplastic initiation and progression. Accordingly, we explored the effect of PIM1 overexpression in 3 different settings: upon hormone treatment, during aging, and in combination with the absence of one Pten allele. We have found that Pim1 overexpression increased the severity of mouse prostate intraepithelial neoplasias (mPIN) moderately in all three settings. Furthermore, Pim1 overexpression, in combination with the hormone treatment, increased inflammation surrounding target tissues leading to pyelonephritis in transgenic animals. Analysis of senescence induced in these prostatic lesions showed that the lesions induced in the presence of inflammation exhibited different behavior than those induced in the absence of inflammation. While high grade prostate preneoplastic lesions, mPIN grades III and IV, in the presence of inflammation did not show any senescence markers and demonstrated high levels of Ki67 staining, untreated animals without inflammation showed senescence markers and had low levels of Ki67 staining in similar high grade lesions. Our data suggest that Pim1 might contribute to progression rather than initiation in prostate neoplasia.

[1306]

**TITULO / TITLE:** The role of heat shock proteins in bladder cancer.

**RESUMEN / SUMMARY:** [Enlace al Resumen / Link to its Summary](1038/nrurol.2013.108)


**AUTORES / AUTHORS:** Ischia J; So Al
Heat shock proteins (HSPs) and clusterin (another chaperone protein with HSP-like properties) are present in normal cells and are upregulated by cellular stressors such as hyperthermia, hypoxia, and cytotoxic agents. HSPs are overexpressed in a wide range of cancers. Cancer cells are in a constant state of proteotoxic stress and exploit the HSPs to protect themselves against the toxic effects of aberrant oncoproteins, genomic instability, hypoxia, and acidosis. In many patients with cancer, high levels of HSPs are associated with poor prognosis and treatment resistance as these proteins protect tumour cells from therapeutic stressors such as androgen or oestrogen withdrawal, radiation, and cytotoxic chemotherapy. Differences in the expression levels of HSPs in bladder cancers compared with normal urothelium have led to HSPs being investigated as diagnostic and prognostic biomarkers. Evidence suggests that HSPs are important modulators of the immune system and have a role in BCG-stimulated regression of urothelial cancers. New bladder cancer treatment strategies that target HSPs are being investigated and could have a synergistic role with modern radiotherapy and chemotherapy regimens. A combination of OGX-427 (an antisense oligonucleotide that targets HSP27), gemcitabine, and cisplatin is currently being investigated in a phase II trial of patients with advanced bladder cancer.

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**TÍTULO / TITLE:** Endocytic adaptor protein epsin is elevated in prostate cancer and required for cancer progression.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


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**AUTORES / AUTHORS:** Tessneer KL; Pasula S; Cai X; Dong Y; Liu X; Yu L; Hahn S; McManus J; Chen Y; Chang B; Chen H

**INSTITUCIÓN / INSTITUTION:** Cardiovascular Biology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK 73104, USA.

**RESUMEN / SUMMARY:** Epsins have an important role in mediating clathrin-mediated endocytosis of ubiquitinated cell surface receptors. The potential role for epsins in tumorigenesis and cancer metastasis by regulating intracellular signaling pathways has largely not been explored. Epsins are reportedly upregulated in several types of cancer including human skin, lung, and canine mammary cancers. However, whether their expression is elevated in prostate cancer is unknown. In this study, we investigated the potential role of epsins in prostate tumorigenesis using the wild type or epsin-deficient human prostate cancer cells, LNCaP, in a human xenograft model, and the spontaneous
TRAMP mouse model in wild type or epsin-deficient background. Here, we reported that the expression of epsins 1 and 2 is upregulated in both human and mouse prostate cancer cells and cancerous tissues. Consistent with upregulation of epsins in prostate tumors, we discovered that depletion of epsins impaired tumor growth in both the human LNCaP xenograft and the TRAMP mouse prostate. Furthermore, epsin depletion significantly prolonged survival in the TRAMP mouse model. In summary, our findings suggest that epsins may act as oncogenic proteins to promote prostate tumorigenesis and that depletion or inhibition of epsins may provide a novel therapeutic target for future prostate cancer therapies.

[1308]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Wiebe C; Nickerson P
INSTITUCIÓN / INSTITUTION: - aPopulation Council, New Delhi, India
bDepartments of Medicine and Immunology, University of Manitoba; Diagnostic Services of Manitoba, Winnipeg, Manitoba, Canada.
RESUMEN / SUMMARY: - PURPOSE OF THE REVIEW: To summarize the evidence supporting the negative impact of de-novo donor-specific antibodies (dnDSA) in renal transplantation and to describe the natural history associated with the development of dnDSA. RECENT FINDINGS: Recent studies have increased our appreciation of the risk factors that predispose to dnDSA while illuminating how these risk factors may relate to the pathophysiology underlying its development. In addition, details regarding the natural history of dnDSA are now available in the context of the different clinical pathologic phenotypes that occur in the patients in whom it develops. Common pitfalls in defining and monitoring dnDSA, when understood, may provide some explanation for the heterogeneity in published studies. SUMMARY: Recognizing that dnDSA is a major cause of late graft loss, and, more importantly, is detectable in many cases long before dysfunction or graft loss occurs, identifies an opportunity to intervene and change the outcome for the patient.

[1309]
TÍTULO / TITLE: - Breast and Prostate Cancer Survivors in a Diabetic Cohort: Results from the Living With Diabetes Study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Wiebe C; Nickerson P
INSTITUCIÓN / INSTITUTION: - aPopulation Council, New Delhi, India
bDepartments of Medicine and Immunology, University of Manitoba; Diagnostic Services of Manitoba, Winnipeg, Manitoba, Canada.
RESUMEN / SUMMARY: - PURPOSE OF THE REVIEW: To summarize the evidence supporting the negative impact of de-novo donor-specific antibodies (dnDSA) in renal transplantation and to describe the natural history associated with the development of dnDSA. RECENT FINDINGS: Recent studies have increased our appreciation of the risk factors that predispose to dnDSA while illuminating how these risk factors may relate to the pathophysiology underlying its development. In addition, details regarding the natural history of dnDSA are now available in the context of the different clinical pathologic phenotypes that occur in the patients in whom it develops. Common pitfalls in defining and monitoring dnDSA, when understood, may provide some explanation for the heterogeneity in published studies. SUMMARY: Recognizing that dnDSA is a major cause of late graft loss, and, more importantly, is detectable in many cases long before dysfunction or graft loss occurs, identifies an opportunity to intervene and change the outcome for the patient.
AUTORES / AUTHORS: - Onitilo AA; Donald M; Stankowski RV; Engel JM; Williams G; Doi SA

INSTITUCIÓN / INSTITUTION: - *School of Population Health, University of Queensland, Brisbane, Queensland, Australia.

RESUMEN / SUMMARY: - Objective Diabetes is more common in cancer survivors than in the general population. The objective of the present study was to determine cancer frequency in a cohort of patients with diabetes and to examine demographic, clinical, and quality of life differences between cancer survivors and their cancer-free peers to inform better individualized care. Methods Self-reported survey data from 3,466 registrants with type 2 diabetes from Australia’s National Diabetes Services Scheme (NDSS) were analyzed to compare relevant variables between cancer survivors and cancer-free patients. Analyses were focused on breast and prostate cancer to reflect the most common cancers in women and men, respectively. Results Five percent of diabetic women reported a history of breast cancer and 4.2% of men reported a history of prostate cancer. Diabetic patients with a history of breast or prostate cancer were older at time of survey and diabetes diagnosis, less likely to report metformin use (women), and more likely to have two or more comorbidities than their cancer-free peers. More diabetic prostate cancer survivors also reported problems with mobility and performing usual tasks. However, cancer-free diabetic subjects reported a lower diabetes-dependent quality of life than diabetic cancer survivors. There was no association between cancer survivorship and duration of diabetes, indices of glycemic control, obesity, or diabetic complications. Conclusions Cancer survivors comprise a significant minority of diabetic patients that are particularly vulnerable and may benefit from interventions to increase screening and treatment of other comorbidities and promote a healthy lifestyle.

[1310]

TÍTULO / TITLE: - Assessing the order of critical alterations in prostate cancer development and progression by IHC: further evidence that PTEN loss occurs subsequent to ERG gene fusion.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Gumuskaya B; Gurel B; Fedor H; Tan HL; Weier CA; Hicks JL; Haffner MC; Lotan TL; De Marzo AM

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, USA.

RESUMEN / SUMMARY: - Background: ERG rearrangements and PTEN (phosphatase and tensin homolog deleted on chromosome 10) loss are two of the most common genetic alterations in prostate cancer. However, there is still
significant controversy regarding the order of events of these two changes during the carcinogenic process. We used immunohistochemistry (IHC) to determine ERG and PTEN status, and calculated the fraction of cases with homogeneous/heterogeneous ERG and PTEN staining in a given tumor.

Methods: Using a single standard tissue section from the index tumor from radical prostatectomies (N=77), enriched for relatively high grade and stage tumors, we examined ERG and PTEN status by IHC. We determined whether ERG or PTEN staining was homogeneous (all tumor cells staining positive) or heterogeneous (focal tumor cell staining) in a given tumor focus. Results: Fifty-seven percent (N=44/77) of tumor foci showed ERG positivity, with 93% of these (N=41/44) cases showing homogeneous ERG staining in which all tumor cells stained positively. Fifty-three percent (N=41/77) of tumor foci showed PTEN loss, and of these 66% (N=27/41) showed heterogeneous PTEN loss. In ERG homogeneously positive cases, any PTEN loss occurred in 56% (N=23/41) of cases, and of these 65% (N=15/23) showed heterogeneous loss. In ERG-negative tumors, 51.5% (N=17/33) showed PTEN loss, and of these 64.7% (N=11/17) showed heterogeneous PTEN loss. In a subset of cases, genomic deletions of PTEN were verified by fluorescence in situ hybridization in regions with PTEN protein loss as compared with regions with intact PTEN protein, which did not show PTEN genomic loss. Conclusions: These results support the concept that PTEN loss tends to occur as a subclonal event within a given established prostatic carcinoma clone after ERG gene fusion. The combination of ERG and PTEN IHC staining can be used as a simple test to ascertain PTEN and ERG gene rearrangement status within a given prostate cancer in either a research or clinical setting.

[1311]
**TÍTULO / TITLE:** - Testicular cancer: New studies identify susceptibility loci, implicated genes.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)


  ●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.121

**AUTORES / AUTHORS:** - Razzak M

[1312]
**TÍTULO / TITLE:** - Genetics: New susceptibility loci for testicular cancer identified.

**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)


  ●●Enlace al texto completo (gratuito o de pago) 1038/nrclinonc.2013.90

[1313]
TÍTULO / TITLE: Prostate cancer: First evidence of somatic STAT5A/B gene amplification.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

TÍTULO / TITLE: Pleiotropy and pathway analyses of genetic variants associated with both type 2 diabetes and prostate cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Raynor L; Pankow JS; Rasmussen-Torvik LJ; Tang W; Prizment A; Couper DJ
INSTITUCIÓN / INSTITUTION: Division of Academic General Pediatrics, Department of Pediatrics, University of Minnesota Minneapolis, MN.
RESUMEN / SUMMARY: AIMS: Epidemiological evidence shows that diabetes is associated with a reduced risk of prostate cancer. The objective of this study was to identify genes that may contribute to both type 2 diabetes and prostate cancer outcomes and the biological pathways these diseases may share. METHODS: The Atherosclerosis Risk in Communities (ARIC) Study is a population-based prospective cohort study in four U.S. communities that included a baseline examination in 1987-89 and three follow-up exams at three year intervals. Participants were 45-64 years old at baseline. We conducted a genomewide association (GWA) study of incident type 2 diabetes in males, summarized variation across genetic loci into a polygenic risk score, and determined if that diabetes risk score was also associated with incident prostate cancer in the same study population. Secondarily we conducted a separate GWA study of prostate cancer, performed a pathway analysis of both type 2 diabetes and prostate cancer, and qualitatively determined if any of the biochemical pathways identified were shared between the two outcomes. RESULTS: We found that the polygenic risk score for type 2 diabetes was not statistically significantly associated with prostate cancer. The pathway analysis also found no overlap between pathways associated with type 2 diabetes and prostate cancer. However, it did find that the growth hormone signaling pathway was statistically significantly associated with type 2 diabetes (p=0.0001). CONCLUSION: The inability of this study to find an association between type 2 diabetes polygenic risk scores with prostate cancer or biological pathways in common suggests that shared genetic variants may not contribute significantly to explaining shared etiology.
TÍTULO / TITLE: SNP-SNP interaction network in angiogenesis genes associated with prostate cancer aggressiveness.
RESUMEN / SUMMARY: Angiogenesis has been shown to be associated with prostate cancer development. The majority of prostate cancer studies focused on individual single nucleotide polymorphisms (SNPs) while SNP-SNP interactions are suggested having a great impact on unveiling the underlying mechanism of complex disease. Using 1,151 prostate cancer patients in the Cancer Genetic Markers of Susceptibility (CGEMS) dataset, 2,651 SNPs in the angiogenesis genes associated with prostate cancer aggressiveness were evaluated. SNP-SNP interactions were primarily assessed using the two-stage Random Forests plus Multivariate Adaptive Regression Splines (TRM) approach in the CGEMS group, and were then re-evaluated in the Moffitt group with 1,040 patients. For the identified gene pairs, cross-evaluation was applied to evaluate SNP interactions in both study groups. Five SNP-SNP interactions in three gene pairs (MMP16+ ROBO1, MMP16+ CSF1, and MMP16+ EGFR) were identified to be associated with aggressive prostate cancer in both groups. Three pairs of SNPs (rs1477908+ rs1387665, rs1467251+ rs7625555, and rs1824717+ rs7625555) were in MMP16 and ROBO1, one pair (rs2176771+ rs333970) in MMP16 and CSF1, and one pair (rs1401862+ rs6964705) in MMP16 and EGFR. The results suggest that MMP16 may play an important role in prostate cancer aggressiveness. By integrating our novel findings and available biomedical literature, a hypothetical gene interaction network was proposed. This network demonstrates that our identified SNP-SNP interactions are biologically relevant and shows that EGFR may be the hub for the interactions. The findings provide valuable information to identify genotype combinations at risk of developing aggressive prostate cancer and improve understanding on the genetic etiology of angiogenesis associated with prostate cancer aggressiveness.

[1316] TÍTULO / TITLE: Genetics: The COGS are turning in breast, ovarian and prostate cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
TÍTULO / TITLE: - Knowledge and perceptions of prostate cancer among Nigerian male immigrants.
RESUMEN / SUMMARY: - Studies focusing on prostate cancer in the Nigerian population, especially Nigerian male immigrants residing in the United States, are limited. Nigerian immigrants are one of the fastest growing populations of Africans currently residing in the United States. According to a report from Migration Policy Institute in Washington DC, 1.4 million African immigrants live in the United States, of which 13.1% or 185,787 are Nigerian-born individuals (Terrazas, 2009). A great number of these African immigrants (159,928/11.3%) currently reside in the Washington metropolitan area. Similar to African American males in the United States, Nigerian men are at high risk for developing prostate cancer. In Nigeria, prostate cancer constitutes 11% of all male cancers making it the #1 ranking cancer among Nigerian men.

TÍTULO / TITLE: - Long-term experience on laparoscopic incontinent urinary diversion unrelated to cystectomy in radiated or recurrent pelvic malignancies.
RESUMEN / SUMMARY: - BACKGROUND: There are few reports describing series of cases about development on laparoscopic urinary diversions no related to cystectomy. The aim of this paper is to show the experience of our reference institutions for treatment of pelvic malignancies when laparoscopic
techniques were applied to perform only urinary diversion without cystectomy or pelvic exenteration. MATERIALS AND METHODS: We included retrospectively 12 cases of cutaneous ureterostomy and 21 cases with a reservoir (16 ileal conduits, 2 colonic conduits and 3 wet colostomies) treated in our institute from 2004 to 2010. It was evaluated operative time, blood loss, intraoperative complications, conversion rate, length of large incision, post operative complications, analgesic consumption, time to food intake, hospital stay, time to recovery to normal activities. Mean time to follow-up was 3(2-7) years. RESULTS: All procedures were completed without conversions. In the cutaneous ureterostomy group the mean surgical time.

[1319] TÍTULO / TITLE: - Small renal masses: A positive surgical margin does not affect survival.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.78
AUTORES / AUTHORS: - Rassweiler JJ; Gozen AS
INSTITUCIÓN / INSTITUTION: - Department of Urology, SLK Kliniken Heilbronn, University of Heidelberg, Am Gesundbrunnen 20, Heilbronn D-7407, Germany.

[1320] TÍTULO / TITLE: - IL-6 expression regulates tumorigenicity and correlates with prognosis in bladder cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0061901
AUTORES / AUTHORS: - Chen MF; Lin PY; Wu CF; Chen WC; Wu CT
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Chang Gung Memorial Hospital, Chiayi, Taiwan ; Chang Gung University, College of Medicine, Taoyuan, Taiwan.
RESUMEN / SUMMARY: - Identification of potential tumor markers will help stratify and identify a tumor’s malignant potential and its response to specific therapies. IL-6 has been reported to be a predictor in various cancers. Therefore, the present study was performed to highlight the role of IL-6 in improving treatment and determining prognosis of bladder cancer. The human bladder cancer cell lines HT1376 and HT1197 were selected for cell and animal experiments, in which biological changes after experimental manipulation of IL-6 were explored, including tumor behavior and related signaling in bladder cancer. In addition, clinical specimens from 85 patients with muscle-invasive, and 50 with non-
muscle invasive bladder cancers were selected for immunohistochemical staining to evaluate the predictive capacity of IL-6 in relation to clinical outcome. The data revealed that IL-6 was overexpressed in the bladder cancer specimens compared with non-malignant tissues at both mRNA and protein levels. Positive staining of IL-6 was significantly correlated with higher clinical stage, higher recurrence rate after curative treatment, and reduced survival rate. Tumor growth and invasive capability were attenuated when IL-6 was blocked. The underlying changes included decreased cell proliferation, less epithelial-mesenchymal transition (EMT), decreased DNA methyltransferase 1 expression and attenuated angiogenesis. In conclusion, our findings showed that IL-6 could be a significant predictor for clinical stage and prognosis of bladder cancer. Moreover, targeting IL-6 may be a promising strategy for treating bladder cancer.
proteins, suggesting that the malignant cells promote the accumulation of M2 TAMs. Furthermore, the tumor-associated milieu as well as isolated TAMs induced the skewing of autologous, blood-derived CD4+ T cells toward a more immunosuppressive phenotype, as shown by decreased production of effector cytokines, increased production of interleukin-10 (IL-10) and enhanced expression of the co-inhibitory molecules programmed death 1 (PD-1) and T-cell immunoglobulin mucin 3 (TIM-3). Taken together, our data suggest that ccRCC progressively attracts macrophages and induces their skewing into M2 TAMs, in turn subverting tumor-infiltrating T cells such that immunoregulatory functions are increased at the expense of effector functions.

[1322]

TÍTULO / TITLE: - Stereotactic body radiotherapy with a focal boost to the MRI-visible tumor as monotherapy for low- and intermediate-risk prostate cancer: early results.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Aluwini S; van Rooij P; Hoogeman M; Kirkels W; Kolkman-Deurloo IK; Bangma C
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Erasmus MC-Daniel den Hoed Cancer Center, Groene Hilledijk, Rotterdam, The Netherlands. s.aluwini@erasmusmc.nl.

RESUMEN / SUMMARY: - BACKGROUND: There is growing evidence that prostate cancer (PC) cells are more sensitive to high fraction dose in hypofractionation schemes. High-dose-rate (HDR) brachytherapy as monotherapy is established to be a good treatment option for PC using extremely hypofractionated schemes. This hypofractionation can also be achieved with stereotactic body radiotherapy (SBRT). We report results on toxicity, PSA response, and quality of life (QOL) in patients treated with SBRT for favorable-risk PC. METHODS: Over the last 4 years, 50 hormone-naive patients with low- and intermediate-risk PC were treated with SBRT to a total dose of 38 Gy delivered in four daily fractions of 9.5 Gy. An integrated boost to 11 Gy per fraction was applied to the dominant lesion if visible on MRI. Toxicity and QoL was assessed prospectively using validated questionnaires.
RESULTS: Median follow-up was 23 months. The 2-year actuarial biochemical control rate was 100%. Median PSA nadir was 0.6 ng/ml. Median International Prostate Symptoms Score (IPSS) was 9/35 before treatment, with a median increase of 4 at 3 months and remaining stable at 13/35 thereafter. The EORTC/RTOG toxicity scales showed grade 2 and 3 gastrointestinal (GI) acute toxicity in 12% and 2%, respectively. The late grade 2 GI toxicity was 3% during 24 months FU. Genitourinary (GU) grade 2, 3 toxicity was seen in 15%, 8%, in
the acute phase and 10%, 6% at 24 months, respectively. The urinary, bowel and sexual domains of the EORTC-PR25 scales recovered over time, showing no significant changes at 24 months post-treatment. CONCLUSIONS: SBRT to 38 Gy in 4 daily fractions for low- and intermediate-risk PC patients is feasible with low acute and late genitourinary and gastrointestinal toxicity. Longer follow-up preferably within randomized studies, is required to compare these results with standard fractionation schemes.

[1323]
TÍTULO / TITLE: - Effect of Small Molecules Modulating Androgen Receptor (SARMs) in Human Prostate Cancer Models.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Tesei A; Leonetti C; Di Donato M; Gabucci E; Porru M; Varchi G; Guerrini A; Amadori D; Arienti C; Pignatta S; Paganelli G; Caraglia M; Castoria G; Zoli W
INSTITUCIÓN / INSTITUTION: - Biosciences Laboratory, IRCCS Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola, Italy.
RESUMEN / SUMMARY: - The management of hormone-refractory prostate cancer represents a major challenge in the therapy of this tumor, and identification of novel androgen receptor antagonists is needed to render treatment more effective. We analyzed the activity of two novel androgen receptor antagonists, (S)-11 and ®-9, in in vitro and in vivo experimental models of hormone-sensitive or castration-resistant prostate cancer (CRPC). In vitro experiments were performed on LNCaP, LNCaP-AR, LNCaP-Rbic and VCaP human prostate cancer cells. Cytotoxic activity was assessed by SRB and BrdU uptake, AR transactivation by luciferase reporter assay and PSA levels by Real Time RT-PCR and ELISA assays. Cell cycle progression-related markers were evaluated by western blot. In vivo experiments were performed on SCID mice xenografted with cells with different sensitivity to hormonal treatment. In hormone-sensitive LNCaP and LNCaP-AR cells, the latter expressing high androgen receptor levels, ®-9 and (S)-11 exhibited a higher cytotoxic effect compared to that of the reference compound (®-bicalutamide), also in the presence of the synthetic androgen R1881. Furthermore, the cytotoxic effect produced by ®-9 was higher than that of (S)-11 in the two hormone-resistant LNCaP-AR and VCaP cells. A significant reduction in PSA levels was observed after exposure to both molecules. Moreover, (S)-11 and ®-9 inhibited DNA synthesis by blocking the androgen-induced increase in cyclin D1 protein levels. In vivo studies on the toxicological profile of ®-9 did not reveal the presence of adverse events. Furthermore, ®-9 inhibited tumor growth in various in vivo
models, especially LNCaP-Rbic xenografts, representative of recurrent disease. Our in vitro results highlight the antitumor activity of the two novel molecules @-9 and (S)-11, making them a potentially attractive option for the treatment of CRPC.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 2147/OTT.S41343
AUTORES / AUTHORS: - Yu XY; Zhang Z; Liu J; Zhan B; Kong CZ
INSTITUCIÓN / INSTITUTION: - Department of Urology, the First Hospital of China Medical University, Shenyang, People’s Republic of China.
RESUMEN / SUMMARY: - BACKGROUND OBJECTIVE: MicroRNAs (miRNAs) are small noncoding RNAs (ribonucleic acids), approximately 22 nucleotides in length, that function as regulators of gene expression. Dysregulation of miRNAs has been associated with the initiation and progression of oncogenesis in humans. The cell division cycle (CDC)25 phosphatases are important regulators of the cell cycle. Their abnormal expression detected in a number of tumors implies that their dysregulation is involved in malignant transformation.
METHODS: Using miRNA target prediction software, we found that miR-141 could target the 3’ untranslated region (3’UTR) sequence of CDC25B. To shed light on the role of miR-141 in renal cell carcinogenesis, the expression of miR-141 was examined by real-time polymerase chain reaction (RT-PCR) in renal cell carcinoma and normal tissues. The impact of miR-141 re-expression on 769-P cells was analyzed using 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and colony-forming assay. A luciferase reporter assay was applied to prove the functionality of the miR-141 binding site. RESULTS: miR-141 is significantly downregulated in renal cell carcinoma. miR-141 re-expression suppressed cell growth in 769-P cells. Luciferase expression from a reporter vector containing the CDC25B-3’UTR was decreased when this construct was transfected with miR-141 in 769-P cells. The overexpression of miR-141 suppressed the endogenous CDC25B protein level in 769-P cells. CONCLUSION: For the first time, we demonstrated that CDC25B is a direct target of miR-141 in renal cell carcinoma. The transcriptional loss of miR-141 and the resultant increase in CDC25B expression facilitates increased genomic instability at an early stage of renal cell carcinoma development.

[1326]
TÍTULO / TITLE: - Post-docetaxel options for further survival benefit in metastatic castration-resistant prostate cancer: Questions of choice.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Asselah J; Sperlich C
INSTITUCIÓN / INSTITUTION: - Medical Oncologist, McGill University Health Centre, Montreal, QC;
RESUMEN / SUMMARY: - There are currently two medical treatments approved in Canada that offer survival benefits for patients with metastatic castration-
resistant prostate cancer that progresses on or after docetaxel-based chemotherapy, and evidence is accumulating on the efficacy of further interventions in this setting. The current and emerging strategies are based on a variety of mechanisms (cytotoxicity, hormonal inhibition, radiopharmacy and immunotherapy) and there is nothing to suggest that patients will be unable to benefit from several or even all of these agents when used sequentially. Given the possibility of multiple lines of treatment for patients whose disease progresses on or after docetaxel, the challenge for clinicians will be to determine the optimum treatment pathway for each individual. That challenge is already being faced, albeit on a limited scale, now that both cabazitaxel (chemotherapy) and abiraterone (hormonal agent) are available for use post-docetaxel.

[1327]
TÍTULO / TITLE: - Differential expression of PRAMEL1, a cancer/testis antigen, during spermatogenesis in the mouse.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Mistry BV; Zhao Y; Chang TC; Yasue H; Chiba M; Oatley J; Diaz F; Liu WS
INSTITUCIÓN / INSTITUTION: - Department of Animal Science, Center for Reproductive Biology and Health (CRBH), College of Agricultural Sciences, The Pennsylvania State University, University Park, PA, USA.
RESUMEN / SUMMARY: - PRAME belongs to a group of cancer/testis antigens (CTAs) that are characterized by their restricted expression in normal gametogenic tissues and a variety of tumors. The PRAME family is one of the most amplified gene families in the mouse and other mammalian genomes. Members of the PRAME gene family encode leucine-rich repeat (LRR) proteins functioning as transcription regulators in cancer cells. However, the role of PRAME in normal gonads is unknown. The objective of this study is to characterize the temporal and spatial expression of the mouse Pramel1 gene, and to determine the cellular localization of the PRAMEL1 protein during the mouse spermatogenesis. Our results indicated that the mouse Pramel1 was expressed in testis only. The mRNA and protein expression level was low in the newborn testes, and gradually increased from 1- to 3-week-old testes, and then remained constant after three weeks of age. Immunofluorescent staining on testis sections with the mouse PRAMEL1 antibody revealed that PRAMEL1 was localized in the cytoplasm of spermatocytes and the acrosomal region of round, elongating and elongated spermatids. Further analyses on the testis squash preparation and spermatozoa at a subcellular level indicated that the
protein localization patterns of PRAMEL1 were coordinated with morphological alterations during acrosome formation in spermatids, and were significantly different in connecting piece, middle piece and principal piece of the flagellum between testicular and epididymal spermatozoa. Collectively, our results suggest that PRAMEL1 may play a role in acrosome biogenesis and sperm motility.

[1328]
TITULO / TITLE: - gp78 is specifically expressed in human prostate cancer rather than normal prostate tissue.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1007/s10735-013-9512-9
AUTORES / AUTHORS: - Shang Y; Zhu Z
INSTITUCIÓN / INSTITUTION: - Tianjin Medical University, Tianjin, 300170, China, yongliangshang@sina.cn.
RESUMEN / SUMMARY: - Elevated expression of gp78 has been observed in many types of cancers including lung, stomach, colon, liver and skin cancer. But there is no report about its expression in prostate cancers. In this study, using immunohistochemical staining we found gp78 is highly expressed in prostate cancers especially early stage tumors, but not in normal prostate tissues. gp78 protein expression is heterogeneous. In some tumors it was expressed in basal cells, while others in stromal cells. For gp78 is a ubiquitin E3 ligase, we then investigated the expression pattern of its cognate E2 (ubiquitin conjugating enzyme)-Ube2g2 in prostate cancers. We found it was expressed in both cancerous and normal tissues of prostate without significant differences in expression level. And unlike gp78, it exhibited a homogeneous expression pattern in different cell types in prostate tissues. In conclusion, our results indicate that gp78 is expressed specifically in human prostate cancer rather than normal prostate tissues, it could be a putative biomarker for prostate cancer diagnosis.

[1329]
TITULO / TITLE: - An unusual combination of extra-adrenal pheochromocytoma and arteriovenous malformation of the ureter in a young adult.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace a la Editora de la Revista http://bmj.com/search.dtl
   ●●Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-009491
AUTORES / AUTHORS: - Khawaja A; Aziz W; Nazim SM; Abbas F
INSTITUCIÓN / INSTITUTION: - Medical College, The Aga Khan University Hospital, Karachi, Sindh, Pakistan.
RESUMEN / SUMMARY: - We present a case of a 24-year-old gentleman who presented with painless pan haematuria for 2 weeks. During the workup, he was diagnosed to have a retrocaval mass after a CT scan while cystoscopy revealed a polypoidal pulsating lesion in the left ureter. After surgical manipulation of the retrocaval mass, the blood pressure of the patient raised to 260/130 mm Hg. It was completely resected and diagnosed as extra-adrenal pheochromocytoma (paraganglioma) after histopathology. The lesion in the ureter was completely excised and fulgurated and diagnosed as an arteriovenous malformation. To the best of our knowledge, this is the first patient to be presented in the literature with this unusual combination.

[1330]

TÍTULO / TITLE: - Prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Outhwaite R
INSTITUCIÓN / INSTITUTION: - St James’s University Hospital, Leeds.

[1331]

TÍTULO / TITLE: - Androgen Receptor Promotes Ligand-Independent Prostate Cancer Progression through c-Myc Upregulation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Gao L; Schwartzman J; Gibbs A; Lisac R; Kleinschmidt R; Wilmot B; Bottomly D; Coleman I; Nelson P; McWeeney S; Alumkal J
INSTITUCIÓN / INSTITUTION: - Division of Hematology/Oncology, Knight Cancer Institute, Oregon Health and Science University, Portland, Oregon, United States of America.
RESUMEN / SUMMARY: - The androgen receptor (AR) is the principal therapeutic target in prostate cancer. For the past 70 years, androgen deprivation therapy (ADT) has been the major therapeutic focus. However, some patients do not benefit, and those tumors that do initially respond to ADT eventually progress. One recently described mechanism of such an effect is growth and survival-promoting effects of the AR that are exerted independently of the AR ligands, testosterone and dihydrotestosterone. However, specific ligand-independent AR target genes that account for this effect were not well characterized. We show
here that c-Myc, which is a key mediator of ligand-independent prostate cancer growth, is a key ligand-independent AR target gene. Using microarray analysis, we found that c-Myc and AR expression levels strongly correlated with each other in tumors from patients with castration-resistant prostate cancer (CRPC) progressing despite ADT. We confirmed that AR directly regulates c-Myc transcription in a ligand-independent manner, that AR and c-Myc suppression reduces ligand-independent prostate cancer cell growth, and that ectopic expression of c-Myc attenuates the anti-growth effects of AR suppression. Importantly, treatment with the bromodomain inhibitor JQ1 suppressed c-Myc function and suppressed ligand-independent prostate cancer cell survival. Our results define a new link between two critical proteins in prostate cancer - AR and c-Myc - and demonstrate the potential of AR and c-Myc-directed therapies to improve prostate cancer control.

TÍTULO / TITLE: - The 786-0 renal cancer cell-derived exosomes promote angiogenesis by downregulating the expression of hepatocyte cell adhesion molecule.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Zhang L; Wu X; Luo C; Chen X; Yang L; Tao J; Shi J

INSTITUCIÓN / INSTITUTION: - Department of Urology, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, P.R. China.

RESUMEN / SUMMARY: - The aims of the current study were to determine whether 7860 renal cancer cell-derived exosomes promote human umbilical vein endothelial cells (HUVECs) to form tubular structures and to uncover the underlying mechanisms associated with this process. Exosomes were extracted and purified using ultrafiltration and sucrose gradient centrifugation and characterized by transmission electron microscopy. Tubular structure formation was observed using the matrigel tubular assay. In addition, an adenovirus vector was used to transfect the hepatocyte cell adhesion molecule (hepaCAM) gene into renal cancer 7860 cells. The expression of hepaCAM and vascular endothelial growth factor (VEGF) mRNA and protein was determined by reverse transcription-polymerase chain reaction and western blot analysis, respectively. Tumor cell-derived exosomes were observed to significantly increase tubular formation in HUVECs. Following transfection with the hepaCAM gene, VEGF expression in 7860 cells was markedly decreased. In HUVECs, exosome treatment increased VEGF mRNA and protein expression, while hepaCAM expression was only decreased at the protein level. In the present study, renal cancer 7860 cell-derived exosomes significantly promoted
angiogenesis via upregulation of VEGF expression in HUVECs, which may be induced by the downregulation of hepaCAM.

[1333]
TÍTULO / TITLE: - Renal cell carcinoma presenting with oral tongue metastasis: a rare case presentation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
     ●●Enlace al texto completo (gratuito o de pago) 4103/0973-1482.110392
AUTORES / AUTHORS: - Ray A; Bhattacharya J; Ganguly S
INSTITUCIÓN / INSTITUTION: - Department of Radiotherapy, NRS Medical College and Hospital, Kolkata, West Bengal, India. amitabh.r@rediffmail.com
RESUMEN / SUMMARY: - Renal cell carcinoma is the most frequent kidney neoplasm, with a high tendency to metastasize. The occurrence of renal carcinoma metastasis to the head and neck region is extremely rare. Here we present one such case where the tongue metastasis was the initial presenting feature of disease.

[1334]
TÍTULO / TITLE: - Oncological outcome after primary prostate cryoablation compared with radical prostatectomy: A single-centre experience.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
     ●●Enlace al texto completo (gratuito o de pago) 3109/21681805.2013.792102
AUTORES / AUTHORS: - Elkjaer MC; Borre M
INSTITUCIÓN / INSTITUTION: - Department of Urology, Aarhus University Hospital, Aarhus, Denmark.
RESUMEN / SUMMARY: - Abstract Objective. The aim of this study was to evaluate the oncological outcome after cryoablation of the prostate (CAP) in localized prostate cancer and to compare the results with those of the established treatment of radical prostatectomy (RP) after 7 years of parallel use. Material and methods. Forty primary, whole-gland CAP procedures performed on 39 patients from 2006 until 2012 at the Department of Urology, Aarhus University Hospital, were prospectively registered. Patients had a minimum of 12 months’ follow-up if they had no recurrent disease. Recurrence was defined by the Phoenix criterion (nadir PSA + 2 ng/ml). Results were compared with oncological outcome in 350 patients who underwent RP over the same period. Results. Median follow-up after CAP was 29.5 (range 4-75) months. Median age at the time of treatment was 65 (47-78) years. A total of 13 (33%) patients developed recurrent disease after CAP, and in D'Amico low-, intermediate- and high-risk subgroups, recurrence was found in two (33%), five (24%) and six
(46%), respectively. Median follow-up after RP was 37 (16-54) months. No cases were excluded. Median age was 64 (34-76) years. Compared with the RP results, where recurrence was found in 62 cases in total (18%), and in three (3%), 30 (21%) and 29(28%) subdivided into risk groups, the risk of recurrent disease was significantly higher after the CAP procedures (p < 0.001).

Conclusions. Recurrence after CAP was high regardless of risk group, indicating a risk of treating and leaving the tumour in situ. Even small low-risk tumours have the potential for recurrence. At this institution, the oncological outcome after CAP was inferior to that after RP.

[1335]

TITULO / TITLE: - A population-based study of tumours of the renal pelvis and ureter: Incidence, aetiology and histopathological findings.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Holmang S; Holmberg E; Johansson SL
INSTITUCIÓN / INSTITUTION: - Department of Urology.
RESUMEN / SUMMARY: - Abstract Objective.Carcinoma of the renal pelvis and ureter are unusual tumours and our limited knowledge comes mainly from case reports and small series from large academic hospitals, as a rule without histopathological review. This study reports aetiological and demographical factors as well as clinicopathological findings of all patients in a large geographical region. Material and methods. All patients in western Sweden with a renal pelvic or ureteral tumour diagnosed between 1971 and 1998 (n = 930) were included. Untreated cases were not excluded. Demographic data and results of preoperative examinations were retrieved from the original clinical records. The histopathological slides were reviewed and tumour stage, grade, configuration, presence of carcinoma in situ and angiolymphatic invasion were determined. Results. The majority of patients (80%) had invasive or high-grade tumours. Carcinoma in situ was present among 30% of patients with non-invasive high-grade tumours. Angiolymphatic invasion (62%) and solid (non-papillary) growth pattern (84%) were very common among patients with stage T2-T4 tumours. Twenty-three women out of 138 (16.7%) with ureteral carcinoma had a history of abdominal radiotherapy for gynaecological cancer 22 years (median) earlier. Forty-one patients out of 930 (4.4%) had a history of abuse of phenacetin-containing analgesics. Conclusions. This study demonstrates a very high incidence of high-grade upper tract tumours with carcinoma in situ, angiolymphatic invasion and solid (non-papillary) growth pattern, which underscores the malignant character of the disease. The possible association between pelvic radiotherapy and ureteral carcinoma warrants further study.
**Title:** Role of oestrogen receptors in bladder cancer development.

**Resumen/Summary:** Early studies documented the existence of sexual dimorphism in bladder cancer occurrence and progression, with a greater bladder cancer incidence in males than females. However, the progression of bladder cancer after diagnosis is much quicker in females than males. These findings can be explained by the effects of female hormones (predominantly oestrogens) and their binding receptors, including oestrogen receptor 1 (ESR1; also known as ERalpha), oestrogen receptor 2 (ESR2; also known as ERbeta), and GPR30 protein on bladder cancer incidence and progression. Results from studies using various in vitro cell lines and in vivo mouse models demonstrate differential roles of oestrogen receptors in cancer initiation and progression. ERalpha suppresses bladder cancer initiation and invasion, whereas ERbeta promotes bladder cancer initiation and progression. Mechanistic studies suggest that ERalpha and ERbeta exert these effects via modulation of the AKT pathway and DNA replication complex, respectively. Targeting these signalling pathways, for example, with ERalpha agonists, ERbeta antagonists, or selective oestrogen receptor modulators such as 4-[2-phenyl-5,7-bis(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-3-yl]phenol (also known as PHTPP), could lead to the development of new therapeutic approaches for controlling bladder cancer progression.
TÍTULO / TITLE: Peptidomimetic targeting of critical androgen receptor-coregulator interactions in prostate cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Ravindranathan P; Lee TK; Yang L; Centenera MM; Butler L; Tilley WD; Hsieh JT; Ahn JM; Raj GV
INSTITUCIÓN / INSTITUTION: Department of Urology, University of Texas Southwestern Medical Center at Dallas, Dallas Texas 75390, USA.
RESUMEN / SUMMARY: The growth of advanced prostate cancer depends on androgen receptor signalling, however treatment options are limited. Here we report the disruption of specific protein-protein interactions involving LXXLL motifs in androgen receptor-coregulator proteins such as PELP1 using a novel, small molecule peptidomimetic (D2). D2 is stable, non-toxic and efficiently taken up by prostate cancer cells. Importantly, D2 blocks androgen-induced nuclear uptake and genomic activity of the androgen receptor. Furthermore, D2 abrogates androgen-induced proliferation of prostate cancer cells in vitro with an IC50 of 40 nM, and inhibits tumour growth in a mouse xenograft model. D2 also disrupts androgen receptor-coregulator interactions in ex vivo cultures of primary human prostate tumours. These findings provide evidence that targeting androgen receptor-coregulator interactions using peptidomimetics may be a viable therapeutic approach for patients with advanced prostate cancer.

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[1339]

TÍTULO / TITLE: Urinary bladder urothelial carcinoma with expression of KIT and PDGFRA and showing diverse differentiations into plasmacytoid, clear cell, acantholytic, nested, and spindle variants, and into adenocarcinoma, signet-ring cell carcinoma, small cell carcinoma, large cell carcinoma, and pleomorphic carcinoma.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Terada T
INSTITUCIÓN / INSTITUTION: Department of Pathology, Shizuoka City Shimizu Hospital Shimizu, Shizuoka, Japan.
RESUMEN / SUMMARY: Various tumors can arise in the urinary bladder (UB); most common is urothelial carcinoma (UC). UC of the UB have many variants. Other types of carcinomas such as adenocarcinoma (AC) and small cell carcinoma (SmCC) can occur in UB carcinomas. Expression of KIT and PDGFRA has not been reported. A 66-year-old man admitted to our hospital because of hematuria. Cystoscopy revealed papillary invasive tumor and a transurethral bladder tumorectomy (TUR-BT) was performed. The TUR-BT
showed UC, AC, SmCC, large cell carcinoma (LCC), and pleomorphic carcinoma (PC). The UC component showed plasmacytoid, spindle, nested, clear cell, anaplastic variants. The AC element showed tubular adenocarcinoma and signet-ring cell carcinoma (Sig). Immunohistochemically, all of these subtypes were positive for cytokeratin (CK) AE1/3, CK CAM5.2, CK34BE12, CK5, CK6, CK7, CK8, CK18, CK19, CK20, EMA, CEA, p63, CA19-9, p53 (positive 45%), MUC1, NSE, NCAM, KIT, PDGFRA, and Ki-67 (87%). They were negative for vimentin, chromogranin, synaptophysin, S100 protein, CD34, CD14, alpha-smooth muscle actin, CD31, caldesmon, CD138, CD45, kappa-chain, lambda-chain, MUC2, MUC5AC and MUC6. Mucin histochemistry revealed mucins in AC element including Sig. A molecular genetic analysis using PCR-direct sequencing method identified no mutations of KIT (exons 9, 11, 13, and 17) and PDGFRA (exons 12 and 18) genes. The carcinoma was highly aggressive and invaded into muscular layer. The nuclear grade was very high, and there were numerous lymphovascular permeations were seen. The surface showed carcinoma in situ involving von-Brunn’s nests. This case shows that carcinoma of UB can show diverse differentiations into numerous histological types and variants, and can express KIT and PDGFRA. The both genes showed no mutations in the present case.

[1340]

TÍTULO / TITLE: - Relationship between Lower Urinary Tract Symptoms/Benign Prostatic Hyperplasia and Metabolic Syndrome in Korean Men.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Park YW; Min SK; Lee JH

INSTITUCIÓN / INSTITUTION: - Department of Urology, National Police Hospital, Seoul, Korea.

RESUMEN / SUMMARY: - PURPOSE: To investigate any associations between lower urinary tract symptoms (LUTS)/benign prostate hyperplasia (BPH) and metabolic syndrome (MetS). MATERIALS AND METHODS: In all, 1,224 male police officers in their 50s who had participated in health examinations were included. LUTS/BPH was assessed by serum prostate-specific antigen, International Prostate Symptom Score (IPSS), transrectal ultrasonography, maximum urinary flow rate (Q max), and postvoid residual urine volume (PVR). In addition, testosterone was also examined. The MetS was defined using NCEP-ATP III guidelines. We used the multiple linear regression test and logistic regression analyses to examine the relationships. RESULTS: MetS was diagnosed in 29.0% of participants. There was no significant difference in the percentage of cases of BPH (IPSS >7, Q max <15 ml/sec, and prostate gland
volume \( \geq 20 \text{ ml} \) (14.2\% in the non-MetS group vs. 17.2 in the MetS group; p value=0.178). The total IPSS score and the Q max were not significantly different. The prostate volume and PVR were significantly greater in the subjects with MetS. After adjusting for age and testosterone, the presence of MetS was not associated with BPH (multivariate odds ratio, 1.122; 95\% confidence interval, 0.593~2.120). Additionally, MetS was not related to IPSS (Beta, -0.189; p value=0.819), prostate volume (Beta, 0.815; p value=0.285), Q max (Beta, -0.827; p value=0.393), or PVR (Beta, 0.506; p value=0.837).

CONCLUSIONS: According to our results, the MetS was not clearly correlated with LUTS/BPH in Korean men in their 50s.

[1341]
TÍTULO / TITLE: - A survey of Sertoli cell differentiation in men after gonadotropin suppression and in testicular cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Tarulli GA; Stanton PG; Loveland KL; Meyts ER; McLachlan RI; Meachem SJ
INSTITUCIÓN / INSTITUTION: - Prince Henry's Institute of Medical Research; Clayton; Victoria, Australia ; Department of Anatomy & Developmental Biology; Monash University; Victoria, Australia.
RESUMEN / SUMMARY: - It is widely held that the somatic cell population that is responsible for sperm development and output (Sertoli cells) is terminally differentiated and unmodifiable in adults. It is postulated, with little evidence, that Sertoli cells are not terminally differentiated in some phenotypes of infertility and testicular cancer. This study sought to compare markers of Sertoli cell differentiation in normospermic men, oligospermic men (undergoing gonadotropin suppression) and testicular carcinoma in situ (CIS) and seminoma samples. Confocal microscopy was used to assess the expression of markers of proliferation (PCNA and Ki67) and functional differentiation (androgen receptor). As additional markers of differentiation, the organization of Sertoli cell tight junction and associated proteins were assessed in specimens with carcinoma in situ. In normal men, Sertoli cells exhibited a differentiated phenotype (i.e., PCNA and Ki67 negative, androgen 40 receptor positive). However, after long-term gonadotropin suppression, 1.7 +/- 0.6\% of Sertoli cells exhibited PCNA reactivity associated with a diminished immunoreactivity in androgen receptor, suggesting an undifferentiated phenotype. Ki67-positive Sertoli cells were also observed. PCNA-positive Sertoli cells were never observed in tubules with carcinoma in situ, and only rarely observed adjacent to seminoma. Tight junction protein localization (claudin 11, JAM-A and ZO-1) was altered in CIS, with a reduction in JAM-A reactivity in Sertoli cells from tubules with CIS and the emergence of strong JAM-A reactivity in seminoma. These
findings indicate that adult human Sertoli cells exhibit characteristics of an undifferentiated state in oligospermic men and patients with CIS and seminoma in the presence of germ cell neoplasia.

[1342]
**TÍTULO / TITLE:** Combined mutation of Vhl and Trp53 causes renal cysts and tumours in mice.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** Albers J; Rajski M; Schonenberger D; Harlander S; Schraml P; von Teichman A; Georgiev S; Wild PJ; Moch H; Krek W; Frew IJ
**INSTITUCIÓN / INSTITUTION:** Institute of Physiology, University of Zurich, Zurich, Switzerland; Competence Center for Systems Physiology and Metabolic Diseases, ETH Zurich and University of Zurich, Zurich, Switzerland.
**RESUMEN / SUMMARY:** The combinations of genetic alterations that cooperate with von Hippel-Lindau (VHL) mutation to cause clear cell renal cell carcinoma (ccRCC) remain poorly understood. We show that the TP53 tumour suppressor gene is mutated in approximately 9% of human ccRCCs. Combined deletion of Vhl and Trp53 in primary mouse embryo fibroblasts causes proliferative dysregulation and high rates of aneuploidy. Deletion of these genes in the epithelium of the kidney induces the formation of simple cysts, atypical cysts and neoplasms, and deletion in the epithelia of the genital urinary tract leads to dysplasia and tumour formation. Kidney cysts display a reduced frequency of primary cilia and atypical cysts and neoplasms exhibit a pro-proliferative signature including activation of mTORC1 and high expression of Myc, mimicking several cellular and molecular alterations seen in human ccRCC and its precursor lesions. As the majority of ccRCC is associated with functional inactivation of VHL, our findings suggest that for a subset of ccRCC, loss of p53 function represents a critical event in tumour development.

[1343]
**TÍTULO / TITLE:** Abiraterone (zytiga), a novel agent for the management of castration-resistant prostate cancer.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** Goldberg T; Berrios-Colon E

[1344]
**TÍTULO / TITLE:** A large mullerian duct cyst presenting as an abdominal mass with ipsilateral renal agenesis: an unusual presentation.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
Symptomatic Mullerian duct cysts are uncommon. A young adult male presented to us with a palpable supra-pubic mass, pain and lower urinary tract symptoms. Initial imaging modalities showed a large cystic lesion in the pelvis with a non-visualized right kidney. A short, blind ending right ureter on retrograde pyelography added to the confusion. On exploration, the lesion was noted to be separate from the seminal vesicles, bladder and posterior urethra. The right kidney was absent. The cystic lesion was excised completely preserving the vas and seminal vesicles. A high index of suspicion is needed for identification of this rare condition. Use of MRI (magnetic resonance imaging) can help improve the diagnostic accuracy. Many a times though, the diagnosis is evident only on exploration.

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Prostate cancer magnetic resonance imaging (MRI): multidisciplinary standpoint.

Prostate cancer is the most common cancer diagnosed in men and a leading cause of death. Accurate assessment is a prerequisite for optimal clinical management and therapy selection of prostate cancer. There are several parameters and nomograms to differentiate between patients with clinically insignificant disease and patients in need of treatment. Magnetic resonance imaging (MRI) is a technique which provides more detailed anatomical images due to high spatial resolution, superior contrast resolution, and multiplanar capability. State-of-the-art MRI techniques, such as diffusion weighted imaging (DWI), MR spectroscopic imaging (MRSI), dynamic contrast enhanced MRI (DCE-MRI), improve interpretation of prostate cancer imaging. In this article, we review the major role of MRI in the advanced management of prostate cancer to noninvasively improve tumor staging, biologic potential,
treatment planning, therapy response, local recurrence, and to guide target biopsy for clinical suspected cancer with previous negative biopsy. Finally, future challenges and opportunities in prostate cancer management in the area of functional MRI are discussed as well.

[1346]
**TÍTULO / TITLE:** Multiparametric magnetic resonance imaging of prostate cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Hedgire SS; Oei TN; McDermott S; Cao K; Patel M Z; Harisinghani MG

**INSTITUCIÓN / INSTITUTION:** Department of Abdominal Imaging and Intervention, Massachusetts General Hospital 55 Fruit St, Boston, 02114 Massachusetts, USA.

**RESUMEN / SUMMARY:** In India, prostate cancer has an incidence rate of 3.9 per 100,000 men and is responsible for 9% of cancer-related mortality. It is the only malignancy that is diagnosed with an apparently blind technique, i.e., transrectal sextant biopsy. With increasing numbers of high-Tesla magnetic resonance imaging (MRI) equipment being installed in India, the radiologist needs to be cognizant about endorectal MRI and multiparametric imaging for prostate cancer. In this review article, we aim to highlight the utility of multiparametric MRI in prostate cancer. It plays a crucial role, mainly in initial staging, restaging, and post-treatment follow-up.

[1347]
**TÍTULO / TITLE:** Can diffusion-weighted magnetic resonance imaging predict a high Gleason score of prostate cancer?

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Shigemura K; Yamanaka N; Yamashita M

**INSTITUCIÓN / INSTITUTION:** Department of Urology, Shinko Hospital, Kobe, Japan; Department of Urology, Kobe University Graduate School of Medicine, Kobe, Japan.

**RESUMEN / SUMMARY:** PURPOSE: To determine the relationship between cancer-positive findings on diffusion-weighted imaging (DWI) magnetic resonance imaging (MRI) and the Gleason score (GS) of radical prostatectomy specimens in prostate cancer (PC). MATERIALS AND METHODS: We performed a retrospective study of 105 consecutive patients with PC who
underwent radical prostatectomy between January 2009 and October 2011 with DWI MRI and full data available for analyses. Prostatectomy specimen pathology included GS, margin status, and capsule invasion, and the clinical factors investigated included age and serum prostate-specific antigen. We investigated the relationship between positive DWI MRI results and these pathological and clinical factors. RESULTS: PC was diagnosed in 62 of 105 patients on DWI MRI. The prostatectomy specimens revealed that the number of cases with GS >4+3 was significantly greater in patients with PC-positive DWI MRI results (34/62, 54.80%) than in those with PC-negative results (2/43, 2.33%; p<0.0001). Positive surgical margins occurred significantly more often in cases with PC-positive DWI MRI results (31/62, 50.0%, compared with 9/43, 21.4%; p=0.0253), and patients with a single tumor lesion in DWI MRI had significantly higher GSs than did those with multiple tumor lesions (p=0.0301). Our statistical results with multiple regression analysis showed that PC-positive DWI MRI results are significantly associated with high GSs. CONCLUSIONS: DWI MRI may help to predict high GSs in prostatectomy specimens. Further studies assessing a greater number of patients will be necessary for a definitive evaluation of DWI MRI as a diagnostic tool for determining PC malignancy.

[1348]
TÍTULO / TITLE: - Small renal masses: Stable long-term renal function after partial nephrectomy in solitary kidney.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Payton S

[1349]
TÍTULO / TITLE: - Comparative expression profiling for human endoplasmic reticulum-resident aminopeptidases 1 and 2 in normal kidney versus distinct renal cell carcinoma subtypes.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Stoehr CG; Buettner-Herold M; Kamphausen E; Bertz S; Hartmann A; Seliger B
INSTITUCIÓN / INSTITUTION: - Institute of Pathology, University Hospital Erlangen Krankenhausstr. 8 - 10, 91054 Erlangen, Germany.
RESUMEN / SUMMARY: - Altered expression of the ER-resident aminopeptidases ERAP1 and ERAP2 might play an important role in shaping the MHC class I-presented peptide repertoire, but their function in tumors has not been determined in detail. Thus, the expression of ERAP1, ERAP2 and HLA class I
heavy chain (HC) was analysed in various renal tumor types and corresponding kidney parenchyma by immunohistochemistry. Additionally, comparative expression profilings of untreated versus interferon (IFN)-gamma-treated RCC cell lines were performed applying qRT-PCR, Western blot and/or flow cytometry. Normal kidney tissues showed strong ERAP1 staining in the proximal tubules of 57.4 % of cases, in the distal tubules of 94.3 % of cases and in the medulla of 88.6 % of cases, whereas high ERAP2 levels were observed in the medulla of 77.1 % of cases and in both, proximal and distal tubules of about 88 % of cases. Imbalanced, downregulated and RCC subtype-specific ERAP1 or ERAP2 expression was detected in 12.7 % or 43.8 % of samples analyzed, respectively. A coordinated downregulation of ERAPs was found in 4.8 %, an upregulation of ERAP1 or ERAP2 in 22.8 % or 2.0 % of RCC lesions. No association exists between ERAP and HLA class I HC expression for any tissue type. A heterogeneous constitutive ERAP expression pattern was also detected in RCC cell lines with lower ERAP2 than ERAP1 expression levels, which was in 11/17 RCC cell lines inducible by IFN-gamma. Conclusively, ERAP1 and ERAP2 might be involved in the development of immune escape mechanisms of RCC.

[1350]

**TITULO / TITLE:** - A case of pediatric paratesticular rhabdomyosarcoma with epididymitis.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


- Enlace al texto completo (gratuito o de pago)

**AUTORES / AUTHORS:** - Kim YJ; Huh JS; Hyun CL; Kim SD

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, School of Medicine, Jeju National University, Jeju, Korea.

**RESUMEN / SUMMARY:** - Paratesticular rhabdomyosarcoma is a rare malignancy arising from the mesenchymal tissues of the spermatic cord, epididymis, testis, and testicular tunica, and accounts for approximately 7% of all rhabdomyosarcomas. It often occurs in children but is known to have a better prognosis than disease at other urogenital sites. Patients typically present with painless unilateral scrotal swelling like a solid testicular tumor. However, we report an unusual case of delayed diagnosis of paratesticular rhabdomyosarcoma accompanied by epididymitis manifesting an painful scrotal swelling.
**TÍTULO / TITLE:** - Low Grade Micropapillary Urothelial Carcinoma, Does It Exist?
- Analysis of Management and Outcomes from the Surveillance, Epidemiology and End Results (SEER) Database.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Vourganti S; Harbin A; Singer EA; Shuch B; Metwalli AR; Agarwal PK

**INSTITUCIÓN / INSTITUTION:** - 1. Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health.

**RESUMEN / SUMMARY:** - Objective: To elucidate the oncologic behavior of Micropapillary Urothelial Bladder Carcinoma (MPBC), a rare aggressive variant histology. Methods: All MPBC patients in SEER 17 database were compared with those with traditional urothelial carcinoma (UC). Kaplan-Meier curves were used to determine OS and CSS. A Cox proportional hazards model (CPH) was constructed to test the effect of covariates on outcomes. Results: From 2001-2008, 120 MPBC patients were identified, 0.1% of all bladder cancer. MPBC presented with more high grade (86.1% vs. 38.7%, p<0.0001) and more high stage disease (40.8% NMI vs. 90.4% NMI, p < 0.0001) than UC. Low grade (LG) NMI MPBC had worse OS and CSS compared to LG UC (p=0.0037, p<0.0001 respectively), and did no better than high grade (HG) NMI MPBC. No difference was detected between HG NMI MPBC and HG NMI UC pts. A CPH model controlling for stage, grade, treatment, age, race, and sex detected no significant survival difference in MPBC vs. UC (HR 1.04, p=0.7966). For NMI MPBC (n=49), only 4 patients underwent definitive therapy, of whom none died of disease. However, in those not receiving definitive therapy (n=45), 7 cancer specific deaths occurred (15.6%). Conclusion: Controlling for stage and grade, no survival difference could be detected between MPBC and UC. Low grade NMI MPBC behaved similarly to both high grade MPBC and high grade UC. We propose that all MPBC (regardless of grade) be managed as high grade disease, and that strong consideration for definitive therapy should be given in all cases.

[1352]

**TÍTULO / TITLE:** - Extensive renal infarction following percutaneous biopsy of a small renal mass: A case report.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Abourbih S; Aldousari S; Brimo F; Omeroglu A; Kassouf W
INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Surgery, McGill University Health Centre, Montreal, QC;

RESUMEN / SUMMARY: - Percutaneous renal biopsy has become increasingly used particularly in patients undergoing active surveillance for small renal masses. We present a patient, who was recently diagnosed with laryngeal squamous cell carcinoma, with significant complication following biopsy of a solid renal mass. The patient was planned for nephron-sparing surgery that was converted to radical nephrectomy due to extensive renal infarction secondary to significant subcapsular hemorrhage inflicted by the biopsy.

[1353]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Esen T; Acar O; Musaoglu A; Vural M; Akpek S

INSTITUCIÓN / INSTITUTION: - School of Medicine, Koc University, Istanbul 34450, Turkey ; Department of Urology, VKF American Hospital, Istanbul 34365, Turkey.

RESUMEN / SUMMARY: - Objectives. To document the feasibility of nephron-sparing surgery (NSS) for the surgical treatment of renal masses measuring larger than 7 cm (cT2) on preoperative imaging. Methods. A total of 139 patients have undergone NSS between 2001 and 2012 by a single surgeon in our clinic. Of these, we identified 17 patients whose tumors were measuring greater than 7 cm on preoperative imaging studies and were limited to the kidney. Their charts were retrospectively reviewed. Results. Mean age of the study population was 49.8 +/- 11.3 years. Thirteen patients were managed by open NSS, while 4 patients have undergone robot-assisted NSS. Mean diameter and mean R.E.N.A.L. score of the tumors that were enucleoresected were 8.2 cm and 8.5, respectively. A total of 5 Clavien grade 2 and higher complications were recorded within 30 days of surgery. Histopathologic examination revealed benign histology in almost ¼ of the cases. After a median followup of 33 months, all of our patients were alive. Only one patient (5.8%) experienced local recurrence. Conclusions. NSS is a feasible and safe option for large (>7 cm) renal masses. It may be considered not only for imperative conditions but also for highly selected cases with a normal contralateral kidney.

[1354]
TÍTULO / TITLE: - The incidence of prostate cancer and urothelial cancer in the prostate in cystoprostatectomy specimens in a tertiary care Canadian centre.

980
RESUMEN / SUMMARY: Radical cystoprostatectomy remains the gold standard treatment for muscle invasive bladder cancer. However, given the treatment related complications of compromised potency and continence with this procedure, prostate/sexuality sparing cystectomy in orthotopic neobladder candidates has emerged in an effort to minimize these quality of life concerns. Recent evidence suggests only a marginal functional benefit from these technical refinements. We sought to determine the incidence of occult prostate cancer and urothelial cancer of the prostate in cystoprostatectomy specimens conducted for muscle invasive bladder cancer.

METHODS: We retrospectively reviewed 83 male patients who underwent radical cystoprostatectomy for muscle invasive bladder cancer between April 2004 and March 2007. The median age of our study group was 71 years. Pathologic findings of prostate/urothelial cancer in the prostate were identified. Clinically significant prostate cancer was defined as Gleason score >6, tumour volume >0.5cc, extracapsular extension or perineural invasion. RESULTS: Our review yielded a 30% (+/-10%, 0.95 CI) rate of prostate cancer, with 19% (+/-8.5%, 0.95 CI) of total specimens being positive for clinically significant prostate cancer. Urothelial cancer in the prostate was identified in 16% (+/-8.5%, 0.95 CI) of patients, with an overlap with prostate cancer in 2 patients. The overall rate of an underlying cancer within the prostate of our cystoprostatectomy specimens was about 46% (+/-10.7%, 0.95 CI). CONCLUSION: These findings suggest that the oncological risk of leaving behind residual cancer may not justify the practice of prostate-sparing cystectomies.

[1355] TÍTULO / TITLE: Molecular imaging and carbonic anhydrase IX-targeted radioimmunotherapy in clear cell renal cell carcinoma.
Conventional imaging is suboptimal at evaluating disease status in renal cell carcinoma (RCC) because of poor sensitivity. Furthermore, there is an unmet need for the treatment of metastatic RCC, both in terms of improvement of progression-free survival and limitation of toxicity. For this reason, radionuclide imaging and radionuclide therapy are extensively investigated. This review provides an overview of the current progress in molecular imaging and radionuclide therapy in clear cell RCC and will focus on promising detection and therapy strategies targeting the carbonic anhydrase IX antigen, which is expressed in clear cell RCC.

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**Erratum to:** Comprehensive overview of the efficacy and safety of sorafenib in advanced or metastatic renal cell carcinoma after a first tyrosine kinase inhibitor.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Afonso FJ; Anido U; Fernandez-Calvo O; Vazquez-Estevez S; Leon L; Lazaro M; Ramos M; Anton-Aparicio L

**INSTITUCIÓN / INSTITUTION:** Complexo Hospitalario Arquitecto Marcide, Ferrol, España.

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**Knockdown of Regulator of Cullins-1 (ROC1) Expression Induces Bladder Cancer Cell Cycle Arrest at the G2 Phase and Senescence.**

**RESUMEN / SUMMARY:** Regulator of Cullins-1 (ROC1) is a key subunit in the Cullin-RING ligase (CRL) protein complex. Overexpression of ROC1 protein is associated with tumor progression and poor prognosis of non-muscle invasive bladder transitional cell carcinoma (NMIBC). This study was designed to assess the effects of ROC1 knockdown in bladder cancer cells and to determine the...
potential mechanisms involved. A total of 112 bladder cancer tissue specimens were recruited for immunohistochemical analyses of ROC1 overexpression. Bladder cancer cell lines were used to knockdown ROC1 expression using ROC1 siRNA. Our data showed that ROC1 knockdown remarkably inhibited bladder cancer cell growth, arrested cells at the G2 phase of the cell cycle, and induced the p53-dependent cell senescence. Molecularly, G2 arrest was associated with upregulation of p21, p27, cyclin B1, and Cdc2 proteins. ROC1 knockdown induced senescence functioned through p53/p21 pathway. Knockdown of p21 expression partially rescued ROC1 knockdown-induced growth inhibition in cancer cells. Furthermore, nude mouse xenograft analyses confirmed these in vitro data. In conclusion, data from the current study indicate that ROC1 plays an essential role in bladder cancer progression and could serve as a novel anticancer target for bladder transitional cell carcinoma (BTCC).

[1358]

**TÍTULO / TITLE:** Decreased expression of miR-430 promotes the development of bladder cancer via the upregulation of CXCR7.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Liu L; Zhao X; Zhu X; Zhong Z; Xu R; Wang Z; Cao J; Hou Y

**INSTITUCIÓN / INSTITUTION:** Department of Urology, Second Xiangya Hospital of Central South University, Changsha, Hunan, P.R. China.

**RESUMEN / SUMMARY:** MicroRNAs (miRNAs) have been demonstrated to be involved in the development of numerous types of malignant tumor. However, the role of miRNA-430 (miR-430) in bladder cancer remains unclear. In the present study, we observed that the expression of miR-430 was significantly downregulated in bladder cancer. Furthermore, the overexpression of miR-430 in human bladder cancer 5637 cells significantly inhibited cell proliferation, migration and colony formation efficiency. These findings were contrary to those obtained following the overexpression of CXCR7, which was found to be a direct target of miR-430 in this study. Further analysis showed that cell proliferation- and migration-related genes, including ERK, matrix metalloproteinase-2 (MMP-2) and MMP-9, were significantly downregulated in miR-430 overexpressed 5637 cells, while they were markedly upregulated in CXCR7 overexpressed 5637 cells. In conclusion, our study reveals important roles of miR-430 and CXCR7 in bladder cancer, and suggests that the downregulation of miR-430 enhances the development of bladder cancer, partly via the upregulation of CXCR7.

RESUMEN / SUMMARY: We examined microRNA-181b (miRNA) expression in prostate cancer tissues and its effect on the prostate cancer cell line PC-3. Tissues from 27 cases of prostate cancer and 30 samples of normal human prostate were collected by surgical removal. Total miRNA was extracted, and the relative expression of miR-181b was quantified using RT-PCR. miR-181b ASO was transfected into prostate cancer PC-3 cells. miR-181b expression in transfected and non-transfected cells was measured using RT-PCR. Changes in cell apoptosis were measured using flow cytometry. MTT and cell growth curve methods were used to assess the influence of miR-181b expression on cell proliferation. The changes in cell invasive ability in vitro were detected using the Transwell chamber method. miR-181b was up-regulated in the prostate cancer tissues compared with the normal prostate samples. It was down-regulated after miR-181b ASO transfection into the prostate cancer PC-3 cells. Down-regulation of miR-181b in the PC-3 cell induced apoptosis, inhibited proliferation, and depressed invasion of PC-3 cells in vitro. As miR-181b is over-expressed in prostate cancer, its down-regulation could have potential as gene therapy for prostate cancer by inducing apoptosis, inhibiting proliferation and depressing invasion by cancer cells.

AUTORES / AUTHORS: He L; Yao H; Fan LH; Liu L; Qiu S; Li X; Gao JP; Hao CQ

INSTITUCIÓN / INSTITUTION: Department of Urology, Chinese PLA General Hospital, Beijing, China.


Enlace al texto completo (gratuito o de pago) 4238/2013.April.2.17

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[1359]

TÍTULO / TITLE: Elevated Jagged-1 and Notch-1 expression in high grade and metastatic prostate cancers.

RESUMEN / SUMMARY: We examined microRNA-181b (miRNA) expression in prostate cancer tissues and its effect on the prostate cancer cell line PC-3. Tissues from 27 cases of prostate cancer and 30 samples of normal human prostate were collected by surgical removal. Total miRNA was extracted, and the relative expression of miR-181b was quantified using RT-PCR. miR-181b ASO was transfected into prostate cancer PC-3 cells. miR-181b expression in transfected and non-transfected cells was measured using RT-PCR. Changes in cell apoptosis were measured using flow cytometry. MTT and cell growth curve methods were used to assess the influence of miR-181b expression on cell proliferation. The changes in cell invasive ability in vitro were detected using the Transwell chamber method. miR-181b was up-regulated in the prostate cancer tissues compared with the normal prostate samples. It was down-regulated after miR-181b ASO transfection into the prostate cancer PC-3 cells. Down-regulation of miR-181b in the PC-3 cell induced apoptosis, inhibited proliferation, and depressed invasion of PC-3 cells in vitro. As miR-181b is over-expressed in prostate cancer, its down-regulation could have potential as gene therapy for prostate cancer by inducing apoptosis, inhibiting proliferation and depressing invasion by cancer cells.

AUTORES / AUTHORS: Zhu H; Zhou X; Redfield S; Lewin J; Miele L

INSTITUCIÓN / INSTITUTION: Cancer Institute, University of Mississippi Medical Center Jackson, MS 39216, USA; Department of Pathology, University of Mississippi Medical Center Jackson, MS 39216, USA.


Enlace al texto completo (gratuito o de pago) 368-78. Print 2013.

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their associations with PCa progression and metastasis. METHODS: Immunohistochemistry (IHC) for Jagged-1 and Notch-1 was performed on tissue microarray (TMA) slides containing 286 formalin-fixed and paraffin-embedded (FFPE) tissue specimens with various prostatic pathologies, including benign changes, high grade prostatic intraepithelial neoplasia (HGPIN), low- and high-grade PCas as well as metastatic PCa. RESULTS: Cytoplasmic and membranous IHC scores for Jagged-1 in both metastatic PCa and high grade PCa were significantly higher than those in low grade PCa and in benign prostatic tissues. Similarly, cytoplasmic IHC scores of Notch-1 in both metastatic PCa and high grade PCa were significantly elevated compared with those observed in low grade PCa and in benign prostatic tissues. A statistically significant correlation was identified between the expression of Jagged-1 and Notch-1 in human prostatic tissues. Furthermore, significantly more highly expressed Jagged-1 in membrane was observed in Caucasian patients with high-grade or metastatic PCa (vs. African Americans) and in PCa patients with positive surgical margins (vs. negative surgical margins). CONCLUSION: Our results provide strong evidence that up-regulation of Jagged1-Notch1 signaling plays a role in PCa progression and metastasis and suggest that Jagged-1 and Notch-1 may be useful markers in distinguishing indolent and aggressive PCas.

[1361]
TÍTULO / TITLE: - Aberrant expression of microRNAs in bladder cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Yoshino H; Seki N; Itesako T; Chiyomaru T; Nakagawa M; Enokida H
INSTITUCIÓN / INSTITUTION: - Department of Urology, Graduate School of Medical and Dental Sciences, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan.
RESUMEN / SUMMARY: - MicroRNAs (miRNAs), a class of small noncoding RNAs, regulate protein-coding gene expression by repressing translation or cleaving RNA transcripts in a sequence-specific manner. A growing body of evidence suggests that miRNAs contribute to bladder cancer development, progression and metastasis. Genome-wide miRNA expression signatures have been used to rapidly and precisely identify aberrant miRNA expression in bladder cancer. Based on reports describing miRNA signatures, several downregulated and upregulated miRNAs have been discovered. Examination of the differential expression of miRNAs between clinical bladder cancer and normal bladder tissue has led to the elucidation of 11 miRNA expression signatures. miRNAs downregulated in bladder cancer, such as miR-145, miR-143 and miR125b, are known to be tumour suppressors, whereas upregulated
miRNAs, such as miR-183, miR-96, miR17-5p and miR-20a are oncogenic. Several studies have demonstrated the potential of miRNAs for providing prognostic information. miR-145 is the most frequently downregulated miRNA in bladder cancer and has been shown to significantly inhibit proliferation, migration and invasion. Understanding the role of differentially expressed miRNAs, as well as their molecular targets, in bladder cancer will provide an effective and promising strategy for miRNA-based therapeutics for the treatment of bladder cancer.

[1362]

**TÍTULO / TITLE:** - Proteoglycan expression in normal human prostate tissue and prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Suhovskih AV; Mostovich LA; Kunin IS; Boboev MM; Nepomnyashchikh GI; Aidagulova SV; Grigorieva EV

**INSTITUCIÓN / INSTITUTION:** - Institute of Molecular Biology and Biophysics SB RAMS, Timakova Street 2, Novosibirsk 630117, Russia.

**RESUMEN / SUMMARY:** - Proteoglycans (PGs) are expressed on the cell surface and extracellular matrix of all mammalian cells and tissues, playing an important role in cell-cell and cell-matrix interactions and signaling. Changes in the expression and functional properties of individual PGs in prostate cancer are shown, although common patterns of PGs expression in normal and tumour prostate tissues remain unknown. In this study, expression of cell surface and stromal proteoglycans (glypican-1, perlecan, syndecan-1, aggrecan, versican, NG2, brevican, decorin, and lumican) in normal tissue and prostate tumours was determined by RT-PCR analysis and immunostaining with core protein- and GAG-specific antibodies. In normal human prostate tissue, versican, decorin, and biglycan were predominant proteoglycans localised in tissue stroma, and syndecan-1 and glypican-1 were expressed mainly by epithelial cells. In prostate tumours, complex changes in proteoglycans occur, with a common trend towards decrease of decorin and lumican expression, overall increase of syndecan-1 and glypican-1 expression in tumour stroma along with its disappearance in tumour epithelial cells, and aggrecan and NG2 expressions in some prostate tumours. All the changes result in the highly individual proteoglycan expression patterns in different prostate tumours, which may be potentially useful as molecular markers for prostate cancer personalised diagnosis and treatment.

[1363]
TÍTULO / TITLE: Iatrogenic Tumor Seeding After Ureteral Stenting in a Dog with Urothelial Carcinoma.

RESUMEN / SUMMARY: A 5 yr old castrated male miniature dachshund presented with clinical signs attributable to carcinoma involving the bladder neck and prostate. On day 84 following diagnosis, the dog developed bilateral ureteral obstruction and ureteral stenting was attempted. The stents were inserted in a normograde fashion via percutaneous puncture of the dilated renal pelvises. Two wk later, the dog developed nodules at both sites of renocentesis. En block resection of the masses was performed, and histologic examination confirmed that the masses were urothelial carcinoma, likely caused by iatrogenic tumor seeding. Ureteral stenting is a useful technique to relieve malignant ureteral obstruction; however, risk of iatrogenic tumor seeding must be considered.

[1364]

TÍTULO / TITLE: Hypoxic Tumor Kinase Signaling Mediated by STAT5A in Development of Castration-Resistant Prostate Cancer.

RESUMEN / SUMMARY: In this study, we hypothesized that androgen-deprivation therapy (ADT) in prostate cancer, although initially efficient, induces changes in the tumor kinome, which subsequently promote development of castration-resistant (CR) disease. Recognizing the correlation between tumor hypoxia and poor prognosis in prostate cancer, we further hypothesized that such changes might be influenced by hypoxia. Microarrays with 144 kinase peptide substrates were applied to analyze CWR22 prostate carcinoma
xenograft samples from ADT-naive, androgen-deprived (AD), long-term AD (ADL), and CR disease stages. The impact of hypoxia was assessed by matching the xenograft kinase activity profiles with those acquired from hypoxic and normoxic prostate carcinoma cell cultures, whereas the clinical relevance was evaluated by analyzing prostatectomy tumor samples from patients with locally advanced disease, either in ADT-naive or early CR disease stages. By using this novel peptide substrate microarray method we revealed high kinase activity mediated by signal transducer and activator of transcription 5α (STAT5A) in CR prostate cancer. Additionally, we uncovered high STAT5A kinase activity already in regressing ADL xenografts, before renewed CR growth was evidenced. Finally, since increased STAT5A kinase activity also was detected after exposing prostate carcinoma cells to hypoxia, we propose long-term ADT to induce tumor hypoxia and stimulate STAT5A kinase activity, subsequently leading to renewed CR tumor growth. Hence, the study detected STAT5A as a candidate to be further investigated for its potential as marker of advanced prostate cancer and as possible therapeutic target protein.

[1365]

TÍTULO / TITLE: - Giant ureteral fibroepithelial polyp presenting as a bladder mass resected ureteroscopically: a case report.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Momenzadeh A; Sarrafzadeh F; Nourbala MH; Saburi A; Telkabadi Z

INSTITUCIÓN / INSTITUTION: - Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, IR Iran.

RESUMEN / SUMMARY: - Primary ureteral neoplasms are very rare and its prevalence is less than 1% of all genitourinary neoplasms. We report a symptomatic giant ureteral fibroepithelial polyp in adult women presenting as a bladder mass which was resected ureteroscopically and reported at the first time from Iran. Cystoscopy is growing use in the treatment of urinary tract lesions Cystoscopy can be used in large lesions in centers with experience rather than open surgery.

[1366]

TÍTULO / TITLE: - Effects of dietary high fat on prostate intraepithelial neoplasia in TRAMP mice.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Increased fat intake is known to be a major cause of prostate cancer. In this study, we investigated the effect of dietary high fat on prostate intraepithelial neoplasia using transgenic adenocarcinoma mouse prostate (TRAMP) mice. Six-week-old male TRAMP mice were fed AIN93G (control group, 4.0 kcal/kg, n=6) and AIN93G-HFD (experimental group, 4.8 kcal/kg, n=7) for 10 weeks. Prostate histopathology, urogenital tract (UGT) weight, epididymal white adipose tissue weight, argyrophilic nucleolar organizer regions (AgNORs) counts, and serum leptin levels were examined. AIN93G-HFD fed group showed progressed neoplastic lesions in the prostate (P<0.05) compared to AIN93G fed group. AIN93G-HFD intake resulted in an increase in the weight of UGT (P<0.05) and epididymal white adipose tissue. The number of Ag-NOR positive dots significantly increased in each prostate lobe and final serum leptin levels in AIN93G-HFD fed group were about twice those of AIN93G fed group (P<0.05). Dietary high fat was related to the prostate cancer progression in the early stage of TRAMP mice and increased serum leptin levels, suggesting that the regulation of dietary components could delay the progression of prostate cancer.

[TITULO / TITLE]: Flaxseed-derived enterolactone is inversely associated with tumor cell proliferation in men with localized prostate cancer.


[Enlace al texto completo (gratuito o de pago)]: 1089/jmf.2012.0159
immunohistochemistry, respectively. After supplementation, we observed significant correlations between intakes of plant lignan and urinary concentrations of total enterolignans (rho=0.677, P<.0001), enterolactone (rho=0.676, P<.0001), and enterodiol (rho=0.628, P<.0001). Importantly, we observed that total urinary enterolignans and enterolactone were significantly and inversely correlated with Ki67 in the tumor tissue (rho=-0.217, P=.011, and rho=-0.230, P=.007, respectively), and a near-significant inverse association was observed for enterodiol (rho=-0.159, P=.064). An inverse association was observed between enterolactone and VEGF (rho=-0.143, P=.141), although this did not reach statistical significance. We did not observe an association between enterolignans and NFκB. In conclusion, flaxseed-derived enterolignans may hinder cancer cell proliferation via VEGF-associated pathways.

[1368]

**TÍTULO / TITLE:** Importance and determinants of Gleason score undergrading on biopsy sample of prostate cancer in a population-based study.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Rapiti E; Schaffar R; Iselin C; Miralbell R; Pelte MF; Weber D; Zanetti R; Neyroud-Caspar I; Bouchardy C

**INSTITUCIÓN / INSTITUTION:** Geneva Cancer Registry, Institute for Social and Preventive Medicine, University of Geneva, 55 boulevard de la Cluse, 1205 Geneva, Switzerland. elisabetta.rapiti@unige.ch.

**RESUMEN / SUMMARY:** BACKGROUND: In this population-based study, we investigated the degree of concordance between Gleason scores obtained from prostate biopsies and those obtained from prostatectomy specimens, as well as the determinants of biopsy understaging. METHODS: We considered for this study all 371 prostate cancer patients recorded at the Geneva Cancer Registry diagnosed from 2004 to 2006 who underwent a radical prostatectomy. We used the kappa statistic to evaluate the Gleason score concordance from biopsy and prostatectomy specimens. Logistic regression was used to determine the parameters that predict the understaging of the Gleason score in prostate biopsies. RESULTS: The kappa statistic between biopsy and prostatectomy Gleason score was 0.42 (p < 0.0001), with 67% of patients exactly matched, and 26% (n = 95) patients with Gleason score underestimated by the biopsy. In a multi-adjusted model, increasing age, advanced clinical stage, having less than ten biopsy cores, and longer delay between the two procedures, were all independently associated with biopsy understaging. In particular, the proportion of exact match increased to 72% when the patients had ten or more needle biopsy cores. The main limitation of the study is that both biopsy and
prostatectomy specimens were examined by different laboratories. CONCLUSIONS: The data show that concordance between biopsy and prostatectomy Gleason scores lies within the classic clinical standards in this population-based study. The number of biopsy cores appears to strongly impact on the concordance between biopsy and radical prostatectomy Gleason score.

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**TÍTULO / TITLE:** Defining a dose-response relationship for prostate external beam radiotherapy.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Trada Y; Plank A; Martin J

**INSTITUCIÓN / INSTITUTION:** School of Medicine, University of Queensland, Brisbane, Australia.

**RESUMEN / SUMMARY:** INTRODUCTION: We aimed to quantify a relationship between radiotherapy dose and freedom from biochemical failure (FFBF) in low- and intermediate-risk prostate cancer. To reduce confounding we used data with a standardised end-point, mature follow-up, low competing risk of metastatic failure, conventional fractionation and separate reporting for outcomes with hormonal therapy (HT). METHODS: A systematic review of the literature was carried out. Studies that reported the use of radiotherapy alone in 1.8-2 Gy fractions in low- and intermediate-risk prostate cancer were included. The primary end-point was Phoenix definition 5-year FFBF. A logistic regression was used to quantify the dose-response relationship. RESULTS: Data from eight studies with 3037 patients met the inclusion criteria. The data from 810 low-risk patients and 2245 intermediate-risk patients were analysed. A strong association between radiotherapy dose and FFBF was found in low- and intermediate-risk patients managed with radiotherapy alone. In low-risk patients not treated with HT the dose required to achieve 50% biochemical tumour control (TCD50) is 52.0 Gy and the slope of the dose-response curve at TCD50 (gamma50) is 2.1%/Gy. At 78 Gy this represented a FFBF of 90.3%. In intermediate-risk patients not treated with HT the TCD50 is 64.7 Gy and gamma50 is 3.2%/Gy. At 78 Gy this translated into a FFBF of 84.3%. HT had a small effect for low-risk patients and an inconsistent effect for intermediate-risk men. CONCLUSION: A strong association was found between radiation dose and biochemical outcome in both low- and intermediate-risk patients. Standardised reporting of results from future studies will make future analyses more robust.

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[1370]
Transjugular renal biopsy in a case of nephrotic syndrome with extrahepatic portal venous obstruction.

Renal biopsy in patients with nephrotic syndrome helps to establish the pathological diagnosis and subsequent treatment. In certain circumstances, biopsies are difficult to obtain because of the risk of bleeding. We report a case where renal biopsy was obtained through the transjugular route in a patient who had nephrotic syndrome with extrahepatic portal venous obstruction.

Kidney function following partial or radical nephrectomy for renal cell carcinoma: A population-based study.

The aim of this retrospective study was to compare kidney function in a population-based cohort of renal cell carcinoma (RCC) patients after partial (PN) or radical nephrectomy (RN). Material and methods. Forty-four consecutive RCC patients who had undergone PN in Iceland between 2000 and 2010 were compared with 44 controls matched for tumour, node, metastasis (TNM) stage who had undergone RN during the same period. Estimated glomerular filtration rate (eGFR) and survival were calculated, and predictors of chronic kidney disease (CKD) were evaluated with multivariate analysis. Results. In 16 cases (36%), PN was performed for imperative reasons (single kidney, decreased kidney function or bilateral kidney tumours) but 28 patients had a normal contralateral kidney. The groups were similar regarding preoperative eGFR, median follow-up and TNM stage, but age and American Society of Anesthesiologists (ASA) score were significantly higher in the RN group. Six months after surgery, eGFR was significantly higher in the PN group. By multivariate analysis, RN contributed negatively to eGFR 6 months after surgery (-12.6 ml/1.73 m2, p <
and increased the risk of new-onset CKD (odds ratio = 3.07, 95% confidence interval 1.03-9.79, p = 0.04), compared to PN. At median follow-up of 44 months, no patients in either group had a recurrence of RCC. The 5-year overall survival (Kaplan-Meier) was 100% and 65% in the PN and RN groups, respectively (log-rank test, p < 0.001). Conclusion. eGFR was significantly lower after RN, and these patients were three times more likely to develop new-onset CKD. These findings suggest that PN successfully preserves kidney function compared to RN, with good oncological outcome and survival.

[1372]
TÍTULO / TITLE: - Prostate cancer: In favour of active surveillance-functional outcomes matter.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Pfister D
INSTITUCIÓN / INSTITUTION: - Department of Urology, University Hospital Aachen, Pauwelsstrasse 30, Aachen 52074, Germany. dpfister@ukaachen.de.

[1373]
TÍTULO / TITLE: - Life expectancy estimates as a key factor in over-treatment: The case of prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Delpierre C; Lamy S; Kelly-Irving M; Molinie F; Velten M; Tretarre B; Woronoff AS; Buemi A; Lapotre-Ledoux B; Bara S; Guizard AV; Colonna M; Grosclaude P
INSTITUCIÓN / INSTITUTION: - Inserm, UMR1027, Toulouse F-31062, France; Universite de Toulouse III, UMR1027, Toulouse F-31062, France. Electronic address: cyrille.delpierre@inserm.fr.
RESUMEN / SUMMARY: - Objective: To estimate the magnitude of over-diagnosis and of potential and actual over-treatment regarding prostate cancer, taking comorbidities into account. Materials and methods: We used a sample collected by the French cancer registries of 1840 cases (T1: 583; T2: 1257) diagnosed in 2001. The proportion of over-diagnosed and over-treated patients was estimated by comparing life expectancy (LE), including or not comorbidities, with natural LE with cancer, using several assumptions from the literature. We distinguished potential and actual over-treatment according to the treatment that patients actually received. Results: Among patients with T1 tumors the
proportion of potential over-treatment using LE adjusted for comorbidity varied from 29.5% to 53.5%, using LE adjusted on comorbidities, and varied from 9.3% to 22.2% regarding actual over-treatment. Between 7.7% and 24.4% of patients receiving a radical prostatectomy, and between 30.8% and 62.5% of those receiving radiotherapy, were over-treated. Among patients with T2 tumors, the proportions of potential and actual over-treatment were 0.9% and 2.0%. Two per cent of patients receiving a radical prostatectomy and 4.9% of those receiving radiotherapy were over-treated. Comorbidities dramatically increased these proportions to nearly 100% of patients, with more than two comorbidities being potentially over-treated and around 33% actually over-treated. Conclusions: According to the French incidence, 3200-4800 French patients may be over-treated, among whom a large proportion of patients had comorbidities. The real issue is to offer the most appropriate treatment to people with low-grade tumors and comorbidities.

[1374]
poorly differentiated tumor in bladder, although rare, it is important to consider large cell neuroendocrine carcinoma in differential diagnosis.

[1375]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 5489/cuaj.248
AUTORES / AUTHORS: - Gondo T; Namiki K; Tanaka A; Yoshioka K; Tanaka M; Yamamoto H; Tachibana M
INSTITUCIÓN / INSTITUTION: - Department of Urology, Tokyo Metropolitan Hiroo Hospital, Tokyo, Japan; ; Department of Urology, Tokyo Medical University, Tokyo, Japan.
RESUMEN / SUMMARY: - An intrascrotal testicular torsion with malignant testicular tumour is extremely rare. We report a case of a 26-year-old male who was diagnosed with testicular torsion by magnetic resonance imaging and with testicular seminoma after orchiectomy. Through this case, we found that if the possibility of testicular torsion remains during the diagnosis of acute scrotum cases, additional examination adding to colour Doppler sonography should be performed. Furthermore, we should be aware of the possibility of testicular tumours during the diagnosis and treatment of acute scrotums. If the affected testis is preserved in the treatment of testicular torsion, a postoperative examination by ultrasound and/or tumour markers for the remaining testis is essential to confirm the absence of testicular tumour.

[1376]
TÍTULO / TITLE: - Curability of Poor-Risk Metastatic Sarcomatoid Renal Cell Carcinoma with the Combination of Gemcitabine, 5-Fluorouracil, and Interferon-Alfa: A Case Report of a 55-Year-Old Man with a 10-Year Complete Remission.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.clgc.2013.04.005
AUTORES / AUTHORS: - Conter HJ; Lim ZD; Ng CS; Millikan RE; Tannir NM
INSTITUCIÓN / INSTITUTION: - Division of Cancer Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX. Electronic address: hjconter@mdanderson.org.

[1377]
TÍTULO / TITLE: - An unusual case of paratesticular mesothelioma on the site of previously excised epididymal adenomatoid tumour.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1016/j.ijscr.2013.02.014
AUTORES / AUTHORS: - Gkentzis A; Sawalem K; Husain J
INSTITUCIÓN / INSTITUTION: - Urology Department, Wigan Infirmary, Wigan, United Kingdom. Electronic address: agapiosgkentzis@hotmail.com.
RESUMEN / SUMMARY: - INTRODUCTION: Malignant paratesticular tumours are rare. We report a case of paratesticular malignant mesothelioma in a patient who had excision of an adenomatoid tumour on the same site in 2 occasions previously. PRESENTATION OF CASE: A middle aged man who had an adenomatoid tumour excised from his left hemiscrotum fifteen years previously was referred with a suspicious left epididymal lump. This was followed up sonographically for 2 years until it showed signs of enlargement and testicular invasion; it was then managed with radical orchidectomy. The histology showed paratesticular epithelioid malignant mesothelioma. The patient was referred to the Oncologists for further management. DISCUSSION: Paratesticular tumours are commonly benign. Scrotal ultrasonography is the preferred diagnostic imaging method. Paratesticular malignant mesotheliomas are very rare and appear to have poor prognosis. The optimal adjuvant treatment post radical orchidectomy is not established yet. In our case there is suggestion of possible malignant transformation from previous adenomatoid tumour. CONCLUSION: In recurrent paratesticular tumours the clinicians should question the possibility of malignant transformation and manage these cases accordingly.

[1378]

TÍTULO / TITLE: - Cardiac metastasis of renal cell carcinoma without inferior vena cava involvement: case report.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Topcuoglu M; Yesilkaya Y; Kilincer A
INSTITUCIÓN / INSTITUTION: - Department of Radiology, Hacettepe University Faculty of Medicine, Ankara, Turkey.
RESUMEN / SUMMARY: - We report the case of a 51-year-old man with advanced renal cell carcinoma (RCC), without inferior vena cava (IVC) involvement, who was treated with chemotherapy. Computed tomography of the thorax and abdomen revealed metastatic invasion of the liver, mediastinal lymph nodes, right adrenal gland, and the head of pancreas. Heart involvement via the IVC is a well-known pattern of metastasis during RCC progression. There are very few cases worldwide that have reported RCC with cardiac metastasis without IVC involvement.

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Título / Title: Temsirolimus in overtreated metastatic renal cancer with subsequent use of sunitinib: A case report.

Resumen / Summary: During the last decade, we have been developing new therapeutic strategies for the treatment of renal cancer, based on knowledge derived from molecular biology. We report a case of long-term renal metastatic cancer progression despite therapy with sunitinib and interleukin, which are the most active drugs in renal cancer. Disease stabilization for 58 weeks was achieved upon sequential use of temsirolimus, following the occurrence of disease progression during angiogenic therapy. The patient demonstrated excellent tolerance without marked symptoms for 10 months. Hypothyroidism and mumps-related adverse events were present. The survival time from diagnosis to lung metastasis was 8 years. Thus, this case demonstrates promising therapeutic effects of the sequential use of tyrosine kinase inhibitors (TKIs) and mammalian target of rapamycin (mTOR) inhibitors during different stages of the disease.

Autor(es) / Authors: Jurado JM; Zarcos I; Delgado M; Blancas I; Legeren M; García-Puche JL

Institución / Institution: Oncology Department, Hospital Clinico Universitario San Cecilio, Avenida, Granada 18012, España.

Resumen / Summary: INTRODUCTION: An embryonic paratesticular rhabdomyosarcoma is a very rare mesenchymal tumor. It is an intrascrotal tumor that is localized in paratesticular structures such as the epididymis or spermatic cord. Rhabdomyosarcoma is most often observed in children and adolescents, presenting as a painless scrotal mass. CASE PRESENTATION: Our patient was an 18-year-old Moroccan man who presented with a painless left scrotal mass that had evolved over four months. An inguinal orchiectomy was performed. A histological examination of the excised tissue revealed an embryonic rhabdomyosarcoma. Our patient had three sessions of chemotherapy.
with vincristine, actinomycin C and cyclophosphamide. Each chemotherapy
session was conducted over five days, with a cycle of 21 days. Our patient was
assessed two months after the last chemotherapy session and demonstrated
good clinical improvement. CONCLUSION: Paratesticular rhabdomyosarcoma
is a rare aggressive tumor manifesting in children and very young adults.
Localized forms have a good prognosis whereas metastatic tumors show very poor results. A well-defined treatment based on surgery and chemotherapy
yields good results.

[1381]
TÍTULO / TITLE: - A case of gallbladder metastasis from a malignant perivascular
epithelioid cell tumor of the bladder.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Sendo H; Harada H; Hasegawa H; Yasuda T; Ohara T;
Oshikiri T; Tanaka K; Fujino Y; Tominaga M
INSTITUCIÓN / INSTITUTION: - Division of Gastroenterological Surgery, Hyogo
Cancer Center.
RESUMEN / SUMMARY: - The perivascular epithelioid cell family of tumors
(PEComas) includes common lesions such as angiomyolipomas,
lymphangioleiomyomas, and clear cell “sugar” tumors of the lung. Less
frequently, PEComas arise in various other locations throughout the body,
including the soft tissue, bone, and the visceral organs. We report the case of a
64-year-old man who underwent total cystectomy because of a primary
malignant PEComa of the bladder in August 2010. The patient was treated with
the mammalian target of rapamycin inhibitor for lung and bone metastasis from
April 2011 and showed stable disease. Computed tomography showed a
growing mass in the neck of the gallbladder 5 months later, which was
suspected to be gallbladder cancer. Cholecystectomy and lymphadenectomy
was performed in February 2012, and histopathological examination indicated
gallbladder metastasis from the primary malignant PEComa of the bladder. This
is, to our knowledge, the first report of malignant PEComa metastasis to the
gallbladder.

[1382]
TÍTULO / TITLE: - Locally advanced paraganglioma of the urinary bladder: a case
report.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
0500-6-156.
AUTORES / AUTHORS: - Beilan J; Lawton A; Hajdenberg J; Rosser CJ
INSTITUCIÓN / INSTITUTION: - Section of Urologic Oncology, MD Anderson Cancer Center Orlando, Orlando, FL 32806, USA. charles.rosser@orlandohealth.com.

RESUMEN / SUMMARY: - BACKGROUND: Paraganglioma of the urinary bladder is a rare tumor. Herein we sought to describe a case of locally advanced paraganglioma of the urinary bladder managed by partial cystectomy and extended pelvic lymph node dissection. CASE PRESENTATION: The case of a 43-year old Haitian male with locally advanced paraganglioma of the urinary bladder is presented in detail. Through surgical extirpation, our patient was rendered disease-free. Eighteen months later the patient is doing well without symptoms but is noted to have subcentimeter bilateral pulmonary nodules and retroperitoneal lymph nodes. No further therapy has been initiated at this time. CONCLUSIONS: Patients with localized tumors have an extremely favorable prognosis and may be managed by less aggressive modalities, whereas patients with metastatic disease have a significant reduced survival rate despite aggressive treatment.

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TÍTULO / TITLE: - Testicular myeloid sarcoma: case report.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Zago LB; Ladeia AA; Etchebehere RM; de Oliveira LR
INSTITUCIÓN / INSTITUTION: - Hospital Dr. Amaral Carvalho, Jau, SP, Brazil.
RESUMEN / SUMMARY: - Myeloid sarcomas are extramedullary solid tumors composed of immature granulocytic precursor cells. In association with acute myeloid leukemia and other myeloproliferative disorders, they may arise concurrently with compromised bone marrow related to acute myeloid leukemia, as a relapsed presentation, or occur as the first manifestation. The testicles are considered to be an uncommon site for myeloid sarcomas. No therapeutic strategy has been defined as best but may include chemotherapy, radiotherapy and/or hematopoietic stem cell transplantation. This study reports the evolution of a patient with testicular myeloid sarcoma as the first manifestation of acute myeloid leukemia. The patient initially refused medical treatment and died five months after the clinical condition started.

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RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
RESUMEN / SUMMARY: - INTRODUCTION: Mantle cell lymphoma is one of the several subtypes of non-Hodgkin’s lymphoma. Mantle cell lymphoma is the rarest of the subtypes, accounting for about 6% of all non-Hodgkin’s lymphoma cases in the United States and Europe. Lymphoid neoplasms of the urinary tract and male genital organs are relatively rare, accounting for less than 5% of extranodal lymphomas. We present a rare case of mantle cell lymphoma infiltrating the ureter causing pelvi-ureteric junction obstruction on tissue diagnosis. CASE PRESENTATION: A 78-year-old Caucasian woman was referred to our department with right flank pain, pyrexia and features of a urinary tract infection. A nephrostogram revealed a grossly distended right pelvicalyceal system in a pelvi-ureteric junction obstruction pattern. She underwent an elective pyeloplasty after her acute management and the results of histological examination revealed mantle cell lymphoma. CONCLUSION: We describe a rare presentation of mantle cell lymphoma as a pelvi-ureteric junction obstruction. To the best of our knowledge, there has not been any previously published report of the above finding. Our patient had a history of a previous lymphoma but the aim of this manuscript is to highlight a possible presentation rather than determining whether the mantle cell lymphoma was de novo or a transformation from her previous splenic lymphoma with villous lymphocytes.

[1385]
TÍTULO / TITLE: - Successful minimally-invasive management of a case of giant prostatic hypertrophy associated with recurrent nephrogenic adenoma of the prostate.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Learney RM; Malde S; Downes M; Shrotri N
INSTITUCIÓN / INSTITUTION: - Department of Urology, Kent & Canterbury Hospital, East Kent Hospitals NHS University Foundation Trust, London, UK. robertheary@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: Benign Prostatic Hypertrophy (BPH) is said to affect at least a third of men over 60. However, the literature contains fewer than 200 reports of prostates over 200g in mass - Giant Prostatic Hypertrophy (GPH). Nephrogenic adenomas are benign lesions of the urinary tract that are believed to represent the local proliferation of shed renal tubular
cells implanting at sites of urothelial injury. CASE PRESENTATION: We present the first case in the literature of these two rare pathologies co-existing in the same patient and the successful management and 36-month follow-up of the patient’s symptoms with minimally invasive therapy, including the still-uncommon selective prostatic artery embolisation. We also briefly discuss the role of PAX2 in injured renal tissues and nephrogenic adenomas.

CONCLUSIONS: Symptomatic Giant Prostatic Hypertrophy (GPH) can be successfully managed with a combination of serial TURPs, 5 alpha-reductase inhibition and selective prostatic artery embolisation (SPAE).

[1386]
TÍTULO / TITLE: - A case of renal angiomyolipoma with intracardiac extension and asymptomatic pulmonary embolism.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Li X; Li Q; Miao Y; Xu H; Liu Y; Qiu X; Wang EH
INSTITUCIÓN / INSTITUTION: - Key Laboratory of Medical Cell Biology, Ministry of Education, China Medical University Shenyang, 110001, China.
RESUMEN / SUMMARY: - ANGIOMYOLIPOMA (AML) IS THE MOST COMMON BENIGN TUMOR OF THE KIDNEY, WHICH IS COMPOSED OF A MIXTURE OF THREE TISSUE COMPONENTS: blood vessels, smooth muscle and adipose cells. Occasionally, AML may extend into the renal vein or the vena cava, but so far at least, intracardiac extension was rarely reported. We herein present one case of renal AML with intracardiac extension and pulmonary embolism simultaneously in a 52-year-old Chinese female patient. Contrast-enhanced computed tomography revealed a well-demarcated heterogeneous mass in the right kidney which extended into the right atrium through the right renal vein and inferior vena cava and resulted in embolization in the right pulmonary artery. The renal mass together with the thrombus was resected. The renal mass and thrombus in vena cava and right atrium shared the similar histological features: mature adipose tissue, smooth muscle and thick-walled vessels. The thrombus in the right pulmonary artery was mainly composed of mature adipose tissue. These histological features and the result of positive immunostaining for HMB-45, Melan-A, and smooth muscle actin supported the diagnosis of AML. The component of epithelioid cells was less than 5% and mitosis was rarely seen. Intracardiac extension is often observed in the malignant tumor and only seldom seen in benign tumors. Our case reminds the rare possibility of intracardiac extension in renal AML, which may potentially result in fatal complications if not appropriately managed.

[1387]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Mori K; Ando T; Nomura T; Sato F; Mimata H

INSTITUCIÓN / INSTITUTION: - Department of Urology, Faculty of Medicine, Oita University, Idaigaoka 1-1, Hasama-cho, Yufu, Oita Prefecture 879-5593, Japan.

RESUMEN / SUMMARY: - Lymphoepithelioma-like carcinoma (LELC) in the bladder is uncommon with a reported incidence of 0.4%-1.3% of all bladder carcinomas. In Japan, some occurrences of LELC have been reported in the renal pelvis and ureter but only two in the bladder. A bladder tumor was identified in a 70-year-old man suffering from macroscopic hematuria for 2 months. Sections of the transurethral tumor resection showed invasive high-grade urothelial carcinoma. The patient was diagnosed with local invasive bladder tumor, and cystectomy with ileal conduit formation was performed. The final pathological evaluation was predominant LELC with urothelial carcinoma. We present a new case of LELC in the bladder and performed a review of all published cases of LELC in the urinary tract to obtain its characteristics and prognostic guide.

[1388]

TÍTULO / TITLE: - Pelvic and muscular metastasis of a renal cell carcinoma: A case report.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - D'Elia C; Cai T; Luciani L; Bonzanini M; Malossini G

INSTITUCIÓN / INSTITUTION: - Departments of Urology, Santa Chiara Hospital, Trento I-938100, Italy.

RESUMEN / SUMMARY: - We report a case of an uncommon site of metastasis of a renal cell carcinoma. The most common sites of renal cell carcinoma metastasis are the lung, lymph nodes, liver, bone and adrenal glands; skeletal muscle metastasis is a rare occurrence. We report the case of a 75-year-old female who underwent a laparoscopic left radical nephrectomy for a renal neoplasm in 2011. The histological examination revealed the presence of a renal cell carcinoma, Fuhrman grade 2, with extensive necrosis and phlogosis areas (TNM 2009 RCC pT2a). Ten months later, the patient noted an indolent swelling on the proximal third of the right thigh and underwent an ultrasonographic and CT evaluation, documenting the presence of a pathological, solid bulk in the front of the right iliac vessels and in the rectus femoris muscle. The fine needle biopsy revealed a metastasis of renal cell...
carcinoma. The patient underwent 4 cycles of sunitinib therapy, followed by 3 cycles of salvage therapy with sorafenib, which were well tolerated. This unpredictable behaviour of RCC suggests the need to perform a thorough follow-up of patients.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Caglia P; Tracia A; Condorelli RA; Calogero AE; Vicari E; Veroux M; Amodeo C; Duca Y; Tracia L; Arcoria AF; Nicoletti C; Mongioi L; LA Vignera S
INSTITUCIÓN / INSTITUTION: - Departments of Surgical Sciences, Organ Transplantation and Advanced Technologies;
RESUMEN / SUMMARY: - Between 2 and 5% of malignant germ cell tumors in males arise at extragonadal sites. The origin of extragonadal retroperitoneal germ cell tumors remains controversial. Whether these develop primarily in the retroperitoneum or are metastases of a primary testicular tumor has long been debated. We report a 38-year-old male who presented with abdominal pain and was diagnosed with retroperitoneal seminoma. The patient gave a history of having undergone a right orchidectomy for an undescended testis via the inguinal route 10 years previously with a reported histology of benign inflammatory mass.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Nesrine M; Sellami R; Doghri R; Rifi H; Raies H; Mezlini A
INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Salah Azaeiz Institute, Tunis 1006, Tunisia.
RESUMEN / SUMMARY: - This paper reports a case of testicular synovial sarcoma with molecular genetic analysis. A 24-year-old male presented with painless scrotal mass. Ultrasonography showed a heterogeneous mass of 66 mm x 34 mm in size involving the inguinal region. Histological examination of a surgical biopsy showed a grade III monophasic growth pattern of spindle cell proliferation. Immunohistochemical analyses indicated positive staining for pancytokeratine and epithelial membrane antigen. Cytogenetic analysis
showed the presence of CYT-SSX1 mutation, and CT scan showed non-specific pleural micro-nodules with a size of 7.5 mm. The patient had an extended left orchidectomy but was lost to follow-up for 1 year. A local recurrent scrotal mass of 32 mm x 25 mm, multiple inguinal lymph nodes, and increased pleural nodules, which were confirmed by histological examination, were treated with three cycles of adriamycin and ifosfamide chemotherapy, surgical resection, and radiotherapy with complete response. After 3 months, the patient developed local recurrence and pulmonary metastases that did not respond to second-line chemotherapy based on gemcitabine and paclitaxel. The patient had dyspnea at the time of this writing and chest pain, and is under third-line chemotherapy based on Deticene after 30 months of following up. This patient died on November 16, 2012 after a resperatory failure and malignant pelural effusion. Synovial sarcoma should be considered in the differential diagnosis of soft tissue tumor and it should be aggressively treated to improve prognosis. Although our patient has shown numerous factors of bad prognosis, he has had a relatively long survival time.

[1391]

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TÍTULO / TITLE: Papillary cystadenoma of epididymis: Is there a need for further investigation in unilateral cases?

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


ENlace al texto completo (gratuito o de pago) 1016/j.ijscr.2013.03.038

AUTORES / AUTHORS: Toutziaris C; Kampantais S; Perdikis I; Gourvas V; Laskaridis L; Gkagkalidis K; Lakis S; Ioannidis S

INSTITUCIÓN / INSTITUTION: 1st Department of Urology, Aristotle University of Thessaloniki, Thessaloniki 54635, Greece.

RESUMEN / SUMMARY: INTRODUCTION: The presence of a mass in the epididymis is not a common entity. The papillary cystadenoma of epididymis is a benign tumor which may occur sporadically or as a characteristic of von Hippel-Lindau disease. PRESENTATION OF CASE: We present a case of a 27-year-old man with a right scrotal mass who was treated with surgical excision. Histopathological examination revealed a clear cell epididymal papillary cystadenoma. A computed tomography scan that was performed later showed no other abnormality or any signs of von Hippel-Lindau disease. DISCUSSION: In this report, a case of a young man suffering from this rare tumor is discussed, focusing on the need of further evaluation in order to determinate if it occurs as a feature of VHL disease or as a sporadic form. CONCLUSION: In unilateral cases of papillary cystadenoma of epididymis such as our patient’s, literature advocates that no further examinations and expensive genetic testing is required.

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1004
Minimally Invasive Pyeloplasty in Horseshoe Kidneys with Ureteropelvic Junction obstruction: A case series.

Background and Purpose: Horseshoe kidney is an uncommon renal anomaly often associated with ureteropelvic junction (UPJ) obstruction. Advanced minimally invasive surgical (MIS) reconstructive techniques including laparoscopic and robotic surgery are now being utilized in this population. However, fewer than 30 cases of MIS UPJ reconstruction in horseshoe kidneys have been reported. We herein report our experience with these techniques in the largest series to date. Materials and Methods: We performed a retrospective chart review of nine patients with UPJ obstruction in horseshoe kidneys who underwent MIS repair at our institution between March 2000 and January 2012. Four underwent laparoscopic, two robotic, and one laparoendoscopic single-site (LESS) dismembered pyeloplasty. An additional two pediatric patients underwent robotic Hellstrom repair. Perioperative outcomes and treatment success were evaluated. Results: Median patient age was 18 years (range 2.5-62 years). Median operative time was 136 minutes (range 109-230 min.) and there were no perioperative complications. After a median follow-up of 11 months, clinical (symptomatic) success was 100%, while radiographic success based on MAG-3 renogram was 78%. The two failures were defined by prolonged t1/2 drainage, but neither patient has required salvage therapy as they remain asymptomatic with stable differential renal function. Conclusions: MIS repair of UPJ obstruction in horseshoe kidneys is feasible and safe. Although excellent short-term clinical success is achieved, radiographic success may be lower than MIS pyeloplasty in heterotopic kidneys, possibly due to inherent differences in anatomy. Larger studies are needed to evaluate MIS pyeloplasty in this population.

A singular case of intravesical bleeding angiomyolipoma in a bladder diverticulum.

Background and Purpose: Horseshoe kidney is an uncommon renal anomaly often associated with ureteropelvic junction (UPJ) obstruction. Advanced minimally invasive surgical (MIS) reconstructive techniques including laparoscopic and robotic surgery are now being utilized in this population. However, fewer than 30 cases of MIS UPJ reconstruction in horseshoe kidneys have been reported. We herein report our experience with these techniques in the largest series to date. Materials and Methods: We performed a retrospective chart review of nine patients with UPJ obstruction in horseshoe kidneys who underwent MIS repair at our institution between March 2000 and January 2012. Four underwent laparoscopic, two robotic, and one laparoendoscopic single-site (LESS) dismembered pyeloplasty. An additional two pediatric patients underwent robotic Hellstrom repair. Perioperative outcomes and treatment success were evaluated. Results: Median patient age was 18 years (range 2.5-62 years). Median operative time was 136 minutes (range 109-230 min.) and there were no perioperative complications. After a median follow-up of 11 months, clinical (symptomatic) success was 100%, while radiographic success based on MAG-3 renogram was 78%. The two failures were defined by prolonged t1/2 drainage, but neither patient has required salvage therapy as they remain asymptomatic with stable differential renal function. Conclusions: MIS repair of UPJ obstruction in horseshoe kidneys is feasible and safe. Although excellent short-term clinical success is achieved, radiographic success may be lower than MIS pyeloplasty in heterotopic kidneys, possibly due to inherent differences in anatomy. Larger studies are needed to evaluate MIS pyeloplasty in this population.

A singular case of intravesical bleeding angiomyolipoma in a bladder diverticulum.
INSTITUCIÓN / INSTITUTION: - Institute of Urology, St. Luke’s Medical Center, Philippines.
RESUMEN / SUMMARY: - Neoplasms arising from intravesical diverticula are rare and considered by urologists as an important surgical challenge. A hamartomatous lesion noted in a bladder diverticulum has never been reported. To our knowledge, we report the first angiomyolipoma, a subtype of mesenchymal hamartoma uncommonly located extrarenally, seen in a bladder dome diverticulum. We discuss the dilemma on the management of such case, related literature and probable etiology.

TÍTULO / TITLE: - A case of the large cell neuroendocrine carcinoma of the urinary bladder.
RESUMEN / SUMMARY: - Large cell neuroendocrine carcinoma (LCNEC) of the urinary bladder is very rare. Definite treatment strategy has not been established and prognosis of the disease is not clear yet. We report a case of primary LCNEC of the urinary bladder here with some review of the literature. The patient was a 84-year-old man. He underwent transurethral resection of bladder tumor (TURBT). Histological examination revealed a rosette arrangement of the tumor cells by HE staining and immunohistochemical study revealed positive CD 56, synaptophysin, and chromogranin A (LCNEC). After TURBT, he has no sign of recurrence for 8 months. We have to strictly observe the progress because LCNEC is very aggressive.

RESUMEN / SUMMARY: - Solitary fibrous tumor is a spindle cell neoplasm mostly originating from pleura; however, it has also recently been reported to be...
A 57-year-old man presented with left lumbal pain. Ultrasonography and computed tomography showed a cystic lesion of 14 x 11 cm with solid areas and septations in middle and lower poles of the left kidney. Radical nephrectomy was performed. Immunohistochemical studies showed strong reactions with CD34 and CD99. A nuclear positivity with Ki-67 was observed in less than 1% of cells. Despite repeated stainings with vimentin, no clear tumor evaluation could be made due to artifacts. The tumor was negative with Bcl-2, desmin, HMB-45, S100, FVIII, and CD31. Histopathological and molecular studies made the diagnosis of a solitary fibrous tumor. The patient is now currently free of disease at the 26th month of followup.

[1396]
TÍTULO / TITLE: - Infarcted adenomatoid tumour of epididymis: a rare case report.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Gupta A; Livingston M; Singh R; Tansey D; Solomon L
INSTITUCIÓN / INSTITUTION: - Urology Department, Queen Alexandra Hospital, Southwick Road, Cosham, Portsmouth PO6 3LY, UK.
RESUMEN / SUMMARY: - Paratesticular tumours are pathologically rare. The vast majority are benign in nature with adenomatoid tumours representing the most common pathological entity. We present the case of a 32-year-old man, from the Indian subcontinent, who presented with a painful scrotal swelling sustained after trauma. The history suggested that the scrotal mass had been present for approximately 12 months, and a preliminary diagnosis of a haemorrhagic cyst caused by trauma was made. Initial management included scrotal support, analgesia, and a follow-up magnetic resonance imaging (MRI) scan. Subsequent imaging and then further histological analysis confirmed a partly necrotic/infarcted adenomatoid tumour of the right epididymis. After scrotal exploration and epididymectomy, the patient made a complete recovery, and, with the histological diagnosis, he was discharged with no further followup. The case is presented as a learning point in the identification and management of such pathologies.

[1397]
TÍTULO / TITLE: - Preoperative hydronephrosis and diabetes mellitus predict poor prognosis in upper urinary tract urothelial carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

●●Enlace al texto completo (gratuito o de pago) 5489/cuaj.11236
INTRODUCTION: We assess the impact of traditional prognostic factors, tumour location, degree of hydronephrosis and diabetes mellitus (DM) on the survival of patients treated for upper urinary tract urothelial carcinoma (UUTUC). METHODS: From January 2004 to March 2010, we analyzed data from 114 patients with UUTUC who underwent nephroureterectomy with a bladder cuff excision. Median patient age was 71 years and median follow-up was 26.5 months. The influence of traditional prognostic factors, including DM, tumour stage, grade, location and degree of hydronephrosis, on recurrence-free survival (RFS) rates were analyzed using Kaplan-Meier analysis and Cox proportional hazards regression model.

RESULTS: Among 61 renal pelvis and 53 ureteral tumour cases, recurrence was identified in 71 cases (62.3%). Kaplan-Meier analysis showed that degree of hydronephrosis was associated with RFS ($p = 0.001$). DM and degree of hydronephrosis were independent factors for RFS in Cox proportional regression analysis (HR=1.8 CI: 1.01-3.55, $p = 0.04$), (HR=3.7, CI: 2.0-6.5, $p = 0.001$). All patients with ureteral tumour had no worse prognosis than those with renal pelvis tumour, but the pT2 patients with ureteral tumour had a worse prognosis than those with renal pelvis tumour with a median RFS of 9 months (range: 2.6-15.3 months) and 29 months (range: 8.0-13.2 months), respectively ($p = 0.028$). CONCLUSIONS: Tumour location is not a factor influencing RFS, except in the pT2 stage. However, severe hydronephrosis is associated with a higher recurrence in UUTUC. Also, DM is related to disease recurrence. Further prospective studies are needed to establish the prognostic significance of DM in large populations.

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**TÍTULO / TITLE:** Primary pediatric stage III renal diffuse large B-cell lymphoma.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


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**AUTORES / AUTHORS:** Hayakawa A; Shimotake N; Kubokawa I; Mitsuda Y; Mori T; Yanai T; Muramaki M; Miyake H; Fujisawa M; Iijima K

**INSTITUCIÓN / INSTITUTION:** Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan.

**RESUMEN / SUMMARY:** BACKGROUND: Although secondary renal involvement of non-Hodgkin lymphoma is frequently encountered, primary renal lymphoma is quite rare. We present a pediatric case of primary renal diffuse large B-cell lymphoma. CASE REPORT: A 12-year-old girl presenting with gross hematuria.
was referred to our hospital. Abdominal ultrasonography and imaging revealed a mass lesion in the superior pole of the right kidney. Serum creatinine and blood urea nitrogen levels were within normal ranges. Preoperative assessment of the mass indicated unspecified renal tumor. Right nephrectomy was performed and pathological examination showed diffuse large B-cell lymphoma. Postoperative fluorodeoxyglucose-positron emission tomography/computed tomography showed a small high-uptake lesion in the thyroid gland and aspiration cytology of the thyroid tumor demonstrated involvement of lymphoma, so stage III tumor diagnosed. After one course of chemotherapy, the patient achieved complete remission. She remains alive without disease, 3 years after completing a total of six courses of chemotherapy. CONCLUSIONS: Primary renal lymphoma is a very rare entity and preoperative diagnosis may be difficult. However, this entity is often reported to show clinically aggressive characteristics and therefore should be considered among the differential diagnoses for unusual renal tumors in pediatric patients.
protruding above the capsular surface. Metastasis was not observed. Cytological examination revealed a population of spindle-shaped cells of variable size, with abundant coarse chromatin and occasionally prominent nucleoli. Initial sections of the kidney were indicative of undifferentiated sarcoma confirmed by immunohistochemistry revealing vimentin-positive and cytokeratin-negative results in all tumour tissues. Additional sections showed very small amounts of both cytokeratin-positive and vimentin-positive areas. DIAGNOSIS: Sarcomatoid renal cell carcinoma (SRCC) with scant epithelial components originating from left kidney. CLINICAL RELEVANCE: Clinical and pathological features were similar to those of human SRCC, even though there was no evidence of metastases. Immunohistochemistry for vimentin and cytokeratin may be useful for definitive diagnosis of renal cell carcinoma with sarcomatoid differentiation, although staining of sections from several different parts of the tumour may be necessary. When a primary renal tumour is presented, SRCC should be considered as this diagnosis may influence treatment protocols and the clinical outcome.

[1400]
TÍTULO / TITLE: - Prostate cancer: Does uptake of technology promote diagnostic testing?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.123

[1401]
TÍTULO / TITLE: - Prostate cancer: Active surveillance in African American men.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.97
AUTORES / AUTHORS: - Moul JW
INSTITUCIÓN / INSTITUTION: - Duke Cancer Institute, Duke University, Durham, NC 27710, USA. judd.moul@duke.edu

[1402]
TÍTULO / TITLE: - Intraarterial chemotherapy with gemcitabine and cisplatin in locally advanced or recurrent squamous cell carcinoma of the penis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 5732/cjc.012.10275
AUTORES / AUTHORS: - Liu JY; Li YH; Liu ZW; Zhang ZL; Ye YL; Yao K; Han H; Qin ZK; Zhou FJ

1010
INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Oncology in South China, Guangzhou, Guangdong 510060, P. R. China. zhoufj@sysucc.org.cn.

RESUMEN / SUMMARY: - The prognosis of locally advanced or recurrent squamous cell carcinoma (SCC) of the penis after conventional treatment is dismal. This study aimed to evaluate the therapeutic effects of intraarterial chemotherapy with gemcitabine and cisplatin in patients with locally advanced or recurrent SCC of the penis. Between April 1999 and May 2011, we treated five patients with locally advanced penile SCC and seven patients with recurrent disease with intraarterial chemotherapy. The response rate and toxicity data were retrospectively analyzed, and survival rates were calculated. After two to six cycles of intraarterial chemotherapy with gemcitabine and cisplatin, one out of five patients with locoregionally advanced disease achieved a complete response (CR), and four patients achieved partial response (PR). Of the seven patients with recurrent disease, two achieved CR, three patients achieved PR, one achieved stable disease, and the other one developed progressive disease. An objective tumor response was therefore achieved in 10 of the 12 patients. The median interval of overall survival for the patients was 24 months (range: 10-50 months). Three out of 10 patients who responded were long-term survivors after intraarterial chemotherapy. Intraarterial chemotherapy with gemcitabine and cisplatin may be effective and potentially curative in locoregionally advanced or recurrent penile SCC. The contribution of this therapy in the primary management of advanced or recurrent penile SCC should be prospectively investigated.

[1403]

TÍTULO / TITLE: - Gelatin-thrombin hemostatic matrix injection to salvage refractory post-renal graft biopsy bleed.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Jain V; Gupta A; Gulia A; Singhal M; Gulati S; Tiwari SC; Kumar A

INSTITUCIÓN / INSTITUTION: - Department of Urology, Robotics and Renal Transplant, Fortis Flt. Lt. Rajan Dhall Hospital, New Delhi, India.

RESUMEN / SUMMARY: - Post-renal biopsy bleeding refractory to angioembolization usually requires graft nephrectomy as a life-saving measure. Gelatin-thrombin hemostatic matrix injection in the needle tract is a novel attempt to control bleeding in such cases and to salvage the allograft. We hereby describe two cases of post-graft biopsy bleed. Both these patients continued to bleed even after angioembolization. They were shifted to the operating room upon developing hypotension, having received multiple blood transfusions with the intention of performing graft nephrectomy to save their
lives. However, bleeding was successfully controlled by using Gelatin-thrombin hemostatic matrix injection in the biopsy needle tract. Patients improved hemodynamically after the procedure. Graft function returned to normal in both the cases. At an average follow-up of 10.4 months, both the patients have shown stable graft functions.

[1404]
**TÍTULO / TITLE:** - Metastatic renal cell carcinoma: how to make the best sequencing decision after withdrawal for intolerance to a tyrosine kinase inhibitor.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Sabbatini R; Ortega C; Procopio G; Masini C; Galligioni E; Porta C

**INSTITUCIÓN / INSTITUTION:** - Department of Oncology & Haematology & Respiratory Disease, University Hospital, Modena, Italy.

**RESUMEN / SUMMARY:** - With seven agents approved for metastatic renal cell carcinoma (RCC) within the past few years, there has undoubtedly been progress in treating this disease. The treatment safety of these new agents, however, now represents a crucial concern, which requires a search for the best possible balance between the minimization of the treatment burden and the need for maintaining appropriate drug dosages able to induce the best clinical benefit. In this review we have analyzed safety data of all approved targeted agents for metastatic RCC available as first- or second-line therapy to provide suggestions aimed at establishing the most appropriate second-line or later treatment on the basis of toxicities that have arisen in therapy. Based on the characteristics and comorbidities of the patients and on the toxicity profile of each treatment, it is possible to plan different therapeutic options. We, therefore, have compiled a list of points that are important to keep in mind when considering the use of the targeted drugs for the treatment of advanced RCC.

[1405]
**TÍTULO / TITLE:** - Metastatic castration-resistant prostate cancer: The emerging continuum of care.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Saad F

**INSTITUCIÓN / INSTITUTION:** - Chairman, National Cancer Institute of Canada Clinical Trials Genitourinary Group (NCIC-CTG G-U) and Canadian Urologic Oncology Group (CUOG); Professor and Chief of Urology, Director of Urologic
Glutathione S-Transferase Polymorphisms (GSTM1, GSTT1 and GSTP1) and Their Susceptibility to Renal Cell Carcinoma: An Evidence-Based Meta-Analysis.

BACKGROUND: The association of the three Glutathione S-transferases (GSTs) polymorphisms (GSTM1, GSTT1 and GSTP1) genotypes with their individual susceptibilities to renal cell carcinoma (RCC) has not been well established. We performed a quantitative meta-analysis to assess the possible associations between the GSTM1, GSTT1 and GSTP1 genotypes and their individual susceptibilities to renal cell carcinoma.

METHODS: We systematically searched the PubMed, CNKI and Embase databases to identify the relevant studies. Finally, 11 eligible studies were selected. The pooled odds ratios (ORs) with their 95% confidence intervals (CIs) were used to assess the association between the GSTs polymorphisms and the risk of RCC. Multiple subgroup analyses and quality assessment of the included studies were performed based on the available information.

RESULTS: None of the GSTs polymorphisms had a significant association with the RCC risk. Similar results were found in the subgroup analyses, except for the GSTs polymorphisms in the situations described below. The GSTM1 and GSTT1 active genotypes in subjects exposed to pesticides (GSTM1: OR = 3.44; 95% CI, 2.04-5.80; GSTT1: OR = 2.84; 95% CI, 1.75-4.60), most of the GSTs genotypes in Asian populations (GSTT1: OR = 2.39, 95% CI = 1.63-3.51; GSTP1: Dominant model: OR = 1.50, 95% CI = 1.14-1.99; Additive model: OR = 1.39, 95% CI = 1.12-1.73; AG vs. AA: OR = 1.47, 95% CI = 1.10-1.97; GG vs. AA: OR = 1.82, 95% CI = 1.07-3.09) and the dual null genotype of GSTT1-GSTP1 (OR = 2.84, 95% CI = 1.75-4.60) showed positive associations with the RCC risk.

CONCLUSION: Our present study provides evidence that the GSTM1, GSTT1 and GSTP1 polymorphisms are not associated with the development of RCC. However, more case-control studies are needed for further confirmation.

[1407]
DNA methylation profile distinguishes clear cell sarcoma of the kidney from other pediatric renal tumors.

A number of specific, distinct neoplastic entities occur in the pediatric kidney, including Wilms’ tumor, clear cell sarcoma of the kidney (CCSK), congenital mesoblastic nephroma (CMN), rhabdoid tumor of the kidney (RTK), and the Ewing’s sarcoma family of tumors (ESFT). By employing DNA methylation profiling using Illumina Infinium HumanMethylation27, we analyzed the epigenetic characteristics of the sarcomas including CCSK, RTK, and ESFT in comparison with those of the non-neoplastic kidney (NK), and these tumors exhibited distinct DNA methylation profiles in a tumor-type-specific manner. CCSK is the most frequently hypermethylated, but least frequently hypomethylated, at CpG sites among these sarcomas, and exhibited 490 hypermethylated and 46 hypomethylated CpG sites in compared with NK. We further validated the results by MassARRAY, and revealed that a combination of four genes was sufficient for the DNA methylation profile-based differentiation of these tumors by clustering analysis. Furthermore, THBS1 CpG sites were found to be specifically hypermethylated in CCSK and, thus, the DNA methylation status of these THBS1 sites alone was sufficient for the distinction of CCSK from other pediatric renal tumors, including Wilms’ tumor and CMN. Moreover, combined bisulfite restriction analysis could be applied for the detection of hypermethylation of a THBS1 CpG site. Besides the biological significance in the pathogenesis, the DNA methylation profile should be useful for the differential diagnosis of pediatric renal tumors.

Application of an interstitial and biodegradable balloon system for prostate-rectum separation during prostate cancer radiotherapy: a prospective multi-center study.

A number of specific, distinct neoplastic entities occur in the pediatric kidney, including Wilms’ tumor, clear cell sarcoma of the kidney (CCSK), congenital mesoblastic nephroma (CMN), rhabdoid tumor of the kidney (RTK), and the Ewing’s sarcoma family of tumors (ESFT). By employing DNA methylation profiling using Illumina Infinium HumanMethylation27, we analyzed the epigenetic characteristics of the sarcomas including CCSK, RTK, and ESFT in comparison with those of the non-neoplastic kidney (NK), and these tumors exhibited distinct DNA methylation profiles in a tumor-type-specific manner. CCSK is the most frequently hypermethylated, but least frequently hypomethylated, at CpG sites among these sarcomas, and exhibited 490 hypermethylated and 46 hypomethylated CpG sites in compared with NK. We further validated the results by MassARRAY, and revealed that a combination of four genes was sufficient for the DNA methylation profile-based differentiation of these tumors by clustering analysis. Furthermore, THBS1 CpG sites were found to be specifically hypermethylated in CCSK and, thus, the DNA methylation status of these THBS1 sites alone was sufficient for the distinction of CCSK from other pediatric renal tumors, including Wilms’ tumor and CMN. Moreover, combined bisulfite restriction analysis could be applied for the detection of hypermethylation of a THBS1 CpG site. Besides the biological significance in the pathogenesis, the DNA methylation profile should be useful for the differential diagnosis of pediatric renal tumors.
RESUMEN / SUMMARY: - Background and purpose: Rectal toxicity presents a significant limiting factor in prostate radiotherapy regimens. This study evaluated the safety and efficacy of an implantable and biodegradable balloon specifically designed to protect rectal tissue during radiotherapy by increasing the prostate—rectum interspace. Patients and methods: Balloons were transperineally implanted, under transrectal ultrasound guidance, into the prostate—rectum interspace in 27 patients with localized prostate cancer scheduled to undergo radiotherapy. Patients underwent two simulations for radiotherapy planning—the first simulation before implant, and the second simulation seven days post implant. The balloon position, the dimensions of the prostate, and the distance between the prostate and rectum were evaluated by CT/US examinations 1 week after the implant, weekly during the radiotherapy period, and at 3 and 6 months post implant. Dose-volume histograms of pre and post implantation were compared. Adverse events were recorded throughout the study period. RESULTS: Four of 27 patients were excluded from the evaluation. One was excluded due to a technical failure during implant, and three patients were excluded because the balloon prematurely deflated. The balloon status was evaluated for the duration of the radiotherapy period in 23 patients. With the balloon implant, the distance between the prostate and rectum increased 10-fold, from a mean 0.22 +/- 0.2 cm to 2.47 +/- 0.47 cm. During the radiotherapy period the balloon length changed from 4.25 +/- 0.49 cm to 3.81 +/- 0.84 cm and the balloon height from 1.86 +/- 0.24 cm to 1.67 +/- 0.22 cm. But the prostate—rectum interspace distance remained constant from beginning to end of radiotherapy: 2.47 +/- 0.47 cm and 2.41 +/- 0.43 cm, respectively. A significant mean reduction in calculated rectal radiation exposure was achieved. The implant procedure was well tolerated. The adverse events included mild pain at the perineal skin and in the anus. Three patients experienced acute urinary retention which resolved in a few hours following conservative treatment. No infections or thromboembolic events occurred during the implant procedure or during the radiotherapy period. CONCLUSION: The transperineal implantation of the biodegradable balloon in patients scheduled to receive radiotherapy was safe and achieved a significant and constant gap between the prostate and rectum. This separation resulted in an important reduction in the rectal radiation dose. A prospective study to evaluate the acute and late rectal toxicity is needed.

[1409]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
OBJECTIVES: Trans-rectal ultrasound (TRUS) is a safe, cost-effective, radiation-free imaging modality for evaluation of prostate. But unfortunately, hemospermia is known to be associated with TRUS-guided prostate biopsy. The aim of this study is to measure the incidence and risk factors of hemospermia in patients undergoing TRUS. PATIENTS AND METHODS: A prospective observational study involving patients undergoing TRUS for suspected prostate cancer has been conducted at Al-Hussein and Sayed Galal Hospitals. Forty patients were included in the study. RESULTS: Most men (90% = 36 patient) undergoing TRUS-guided prostatic biopsy, who were able to ejaculate, experienced hemospermia, which was associated with some degree of anxiety. The mean duration of hemospermia was 4 (+/-1.4) weeks. The number of ejaculations before the complete resolution of hemospermia was 6 (+/-5.6). None of the clinical and pathological factors was a significant predictor of the duration of hemospermia. CONCLUSION: Patients should be adequately counseled before TRUS-guided prostatic biopsy to avoid anxiety and alterations in sexual activity.

[1410]


RESUMEN / SUMMARY: - El objetivo del presente trabajo es descubrir la técnica quirúrgica basada en asistencia robótica para la nefron-sparing surgery. Realizamos una revisión retrospectiva de nuestra serie de 32 pacientes consecutivos (2 con 2 tumores y uno con 4 bilaterales tumores), para a...
total of 37 robotic nephron-sparing surgery (RNSS) performed between June 2008 and July 2012 by a single surgeon (G.C.). The technique differs depending on tumor site and size. The mean tumor size was 3.6 cm; according to the R.E.N.A.L. Nephrometry Score 9 procedures were considered of low, 14 of moderate and 9 of high complexity with no conversion in open surgery. Vascular clamping was performed in 22 cases with a mean warm ischemia time of 21.5 min and the mean total procedure time was 149.2 min. Mean estimated blood loss was 187.1 ml. Mean hospital stay was 4.4 days. Histopathological evaluation confirmed 19 cases of clear cell carcinoma (all the multiple tumors were of this nature), 3 chromophobe tumors, 1 collecting duct carcinoma, 5 oncocytoamas, 1 leiomyoma, 1 cavernous haemangioma and 2 benign cysts. Associated surgical procedures were performed in 10 cases (4 cholecystectomies, 3 important lyses of peritoneal adhesions, 1 adnexectomy, 1 right hemicolecction, 1 hepatic resection). The mean follow-up time was 28.1 months +/- 12.3 (range 6-54). Intraoperative complications were 3 cases of important bleeding not requiring conversion to open or transfusions. Regarding post-operative complications, there were a bowel occlusion, 1 pleural effusion, 2 pararenal hematomas, 3 asymptomatic DVT (deep vein thrombosis) and 1 transient increase in creatinine level. There was no evidence of tumor recurrence in the follow-up. RNSS is a safe and feasible technique. Challenging situations are hilar, posterior or intraparenchymal tumor localization. In our experience, robotic technology made possible a safe minimally invasive management, including vascular clamping, tumor resection and parenchyma reconstruction.

[1411] TÍTULO / TITLE: - Urinary high molecular weight matrix metalloproteinases as non-invasive biomarker for detection of bladder cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Mohammed MA; Seleim MF; Abdalla MS; Sharada HM; Abdel Wahab AH
INSTITUCIÓN / INSTITUTION: - Department of Cancer Biology, National Cancer Institute, Cairo University, Cairo, Egypt. abdelhadya@gmail.com.
RESUMEN / SUMMARY: - BACKGROUND: Matrix Metalloproteinases (MMPs) are key molecules for tumor growth, invasion and metastasis. Over-expression of different MMPs in tumor tissues can disturb the homeostasis and increase the level of various body fluids. Many MMPs including high molecular weights (HMWs) were detected in the urine of prostate and bladder cancer patients. Our aim here is to assess the usefulness of HMW MMPs as non invasive biomarkers in bilharzial bladder cancer in Egyptian patients. METHODS: The
activity of different MMPs including HMW species was determined using zymographic analysis technique in the urine samples procured from sixty six bladder cancer patients (bilharzial and non-bilharzial) as well as hundred healthy control subjects. Also, the correlation between these HMW MMPs activities and different clinico-pathological parameters was investigated.

RESULTS: High frequency of urine MMPs (uMMPs) activity was determined in 63.6% of examined tumor cases, however, none of the control cases showed any uMMPs activity. MMP-9 had the highest activity (62%) followed by MMP9/NGAL (60%), MMP-2 (54.5%), MMP-9 dimer (53%), ADAMTS (25.6%), and the lowest one was MMP-9/TIMP-1 (12%) only. There was no correlation between uMMPs and any of clinico-pathological parameters including age, gender, tumor size and type, bilharziasis, grade, lymph node involvement, and invasion to the prostate. A significant correlation was established only between MMP-9/TIMP-1 activities with the tumor size. CONCLUSIONS: This study revealed that the detection of urinary MMPs including HMWs activity might be sensitive biomarkers for prediction of bladder cancer. It is also demonstrate that the detection of these urinary HMW gelatinases could not differentiate between bilharzial and non bilharzial bladder cancer subtypes.
RESUMEN / SUMMARY: - Rational-designed multimerization of targeting ligands can be used to improve kinetic and thermodynamic properties. Multimeric targeting ligands may be produced by tethering multiple identical or two or more monomeric ligands of different binding specificities. Consequently, multimeric ligands may simultaneously bind to multiple receptor molecules. Previously, multimerization has been successfully applied on radiolabeled RGD peptides, which resulted in an improved tumor targeting activity in animal models. Multimerization of peptide-based ligands may improve the binding characteristics by increasing local ligand concentration and by improving dissociation kinetics. Here, we present a preclinical study on a novel radiolabeled bombesin (BN) homodimer, designated \(\text{In-DOTA-[(Aca-BN(7-14))]_2}\), that was designed for enhanced targeting of gastrin-releasing peptide receptor (GRPR)-positive prostate cancer cells. A BN homodimer was conjugated with DOTA-NHS and labeled with \(\text{In}\). After HPLC purification, the GRPR targeting ability of \(\text{In-DOTA-[(Aca-BN(7-14))]_2}\) was assessed by microSPECT imaging in SCID mice xenografted with the human prostate cancer cell line PC-3. \(\text{In}\) labeling of DOTA-[Aca-BN(7-14)]2 was achieved within 30 min at 85 degrees C with a labeling yield of >40%. High radiochemical purity (>95%) was achieved by HPLC purification. \(\text{In-DOTA-[(Aca-BN(7-14))]_2}\) specifically bound to GRPR-positive PC-3 prostate cancer cells with favorable binding characteristics because uptake of \(111\text{In-DOTA-[(Aca-BN(7-14))]_2}\) in GRPR-positive PC-3 cells increased over time. A maximum peak with 30% radioactivity was observed after 2 h of incubation. The log D value was 1.8 +/- 0.1. \(111\text{In-DOTA-[(Aca-BN(7-14))]_2}\) was stable in vitro both in PBS and human serum for at least 4 days. In vivo biodistribution analysis and microSPECT/CT scans performed after 1, 4, and 24 h of injection showed favorable binding characteristics and tumor-to-normal tissue ratios. This study identifies \(111\text{In-DOTA-[(Aca-BN(7-14))]_2}\) as a promising radiotracer for nuclear imaging of GRPR in prostate cancer.

[1414]

TÍTULO / TITLE: - Molecular Mechanisms of Silibinin-Mediated Cancer Chemoprevention with Major Emphasis on Prostate Cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ting H; Deep G; Agarwal R

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA.
RESUMEN / SUMMARY: - Despite advances in early detection, prostate cancer remains the second highest cancer mortality in American men, and even successful interventions are associated with enormous health care costs as well as prolonged deleterious effects on quality of patient life. Prostate cancer chemoprevention is one potential avenue to alleviate these burdens. It is a regime whereby long-term treatments are intended to prevent or arrest cancer development, in contrast to more direct intervention upon disease diagnosis. Based on this intention, cancer chemoprevention generally focuses on the use of nontoxic chemical agents which are well-tolerated for prolonged usage that is necessary to address prostate cancer’s multistage and lengthy period of progression. One such nontoxic natural agent is the flavonoid silibinin, derived from the milk thistle plant (Silybum marianum), which has ancient medicinal usage and potent antioxidant activity. Based on these properties, silibinin has been investigated in a host of cancer models where it exhibits broad-spectrum efficacy against cancer progression both in vitro and in vivo without noticeable toxicity. Specifically in prostate cancer models, silibinin has shown the ability to modulate cell signaling, proliferation, apoptosis, epithelial to mesenchymal transition, invasion, metastasis, and angiogenesis, which taken together provides strong support for silibinin as a candidate prostate cancer chemopreventive agent.

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[1415]
TÍTULO / TITLE: - Advances in bladder cancer imaging.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1186/1741-7015-11-104
AUTORES / AUTHORS: - Hafeez S; Huddart R
INSTITUCIÓN / INSTITUTION: - The Royal Marsden NHS Foundation Trust and the Institute of Cancer Research, Sutton, Surrey, UK. Robert.huddart@rmh.nhs.uk.
RESUMEN / SUMMARY: - The purpose of this article is to review the imaging techniques that have changed and are anticipated to change bladder cancer evaluation. The use of multidetector 64-slice computed tomography (CT) and magnetic resonance imaging (MRI) remain standard staging modalities. The development of functional imaging such as dynamic contrast-enhanced MRI, diffusion-weighted MRI and positron emission tomography (PET)-CT allows characterization of tumor physiology and potential genotypic activity, to help stratify and inform future patient management. They open up the possibility of tumor mapping and individualized treatment solutions, permitting early identification of response and allowing timely change in treatment. Further validation of these methods is required however, and at present they are used in conjunction with, rather than as an alternative to, conventional imaging techniques.
TÍTULO / TITLE: - Regulation network analysis of testicular seminoma at various stages of progression.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 4238/2013.March.11.11
AUTORES / AUTHORS: - Sha JJ; Dong YH; Liu DM; Bo JJ; Huang YR; Li Z; Ping P
INSTITUCIÓN / INSTITUTION: - Department of Urology, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China.
RESUMEN / SUMMARY: - Testicular seminoma has become the most common solid malignancy in young men, especially in the 20s group. We obtained the gene expression profile of human testicular seminoma cells from NCBI, identified the differentially expressed genes of testicular seminoma cells of different stages, and constructed the regulation networks of different stages of testicular seminoma using bioinformatics methodology. Forty differentially expressed genes of testicular seminoma cells of different stages were identified. These genes and pathways are apparently involved in the progression of testicular seminoma.

TÍTULO / TITLE: - Antitumor activity of a polysaccharide from Pleurotus eryngii on mice bearing renal cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.carbpol.2013.03.024
AUTORES / AUTHORS: - Yang Z; Xu J; Fu Q; Fu X; Shu T; Bi Y; Song B
INSTITUCIÓN / INSTITUTION: - Department of Urology, Tangdu Hospital, the Fourth Military Medical University, Xi’an, China.
RESUMEN / SUMMARY: - One water-soluble polysaccharide (PEPw), with an average molecular weight of 2.5x10(4)Da, was isolated from the fruiting bodies of Pleurotus eryngii and subjected to composition analysis and evaluated for the antitumor and immunomodulatory activity. PEPw was composed of arabinose, mannose and galactose in a molar ratio of 1.2:2.3:6.2 and had a backbone mainly consisting of 1,6-linked-Galp, 1,2,6-linked-Galp and 1,4-linked-Manp residues, which was occasionally terminated with terminal-Araf attached to O-2 of 1,2,6-linked-Galp residue. The animal experiment results showed that PEPw significantly increased relative thymus and spleen indices, promoted the spleen lymphocytes proliferation induced by ConA or LPS, elevated the activities of NK cell and CTL in spleen, and increased the serum concentration of TNF-alpha.
and IL-2 in Renca tumor-bearing mice. As a result, the tumor growth was significantly inhibited by PEPw treatment at the doses of 50, 100 and 200mg/kg in a dose-dependent manner. These data indicated that the anti-tumor activity of PEPw may be related to the activation of the immune response in tumor-bearing mice.

[1418]
TÍTULO / TITLE: - NVP-LDE-225 (Erismodegib) inhibits epithelial-mesenchymal transition and human prostate cancer stem cell growth in NOD/SCID IL2Rgamma null mice by regulating Bmi-1 and microRNA-128.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Oncogenesis. 2013 Apr 8;2:e42. doi: 10.1038/oncsis.2013.5.
AUTORES / AUTHORS: - Nanta R; Kumar D; Meeker D; Rodova M; Van Veldhuizen PJ; Shankar S; Srivastava RK
INSTITUCIÓN / INSTITUTION: - Department of Pharmacology, Toxicology and Therapeutics, and Medicine, The University of Kansas Cancer Center, The University of Kansas Medical Center, Kansas City, KS, USA.
RESUMEN / SUMMARY: - Prostate cancer stem cells (CSCs) are defined by their extensive self-renewal, differentiation and tumor initiation properties. It is now clear that CSCs are involved in tumor growth and recurrence, and resistance to conventional treatments. The sonic hedgehog (Shh) pathway has a crucial role in stemness and tumorigenesis. Thus, the strategy that suppresses stemness and consequently tumorigenic potential of CSCs could be considered for the management of prostate cancer. The objectives of this study were to examine the molecular mechanisms, by which NVP-LDE-225/Erismodegib (smoothened inhibitor) regulates stem cell characteristics and tumor growth in prostate cancer. The effects of NVP-LDE-225 on CSC’s viability, sphere formation, apoptosis, epithelial-mesenchymal transition (EMT) and tumor growth in NOD/SCID IL2Rgamma null mice were examined. NVP-LDE-225 inhibited cell viability and spheroid formation, and induced apoptosis by activation of caspase-3 and cleavage of poly-ADP ribose polymerase (PARP). NVP-LDE-225 induced expression of Bax and Bak, and inhibited the expression of Bcl-2, Bcl-XL, XIAP, cIAP1, cIAP2 and survivin. NVP-LDE-225 inhibited Gli transcriptional activity, Gli-DNA interaction and the expression of Gli1, Gli2, Patched1 and Patched-2 in prostate CSCs. Interestingly, NVP-LDE-225 induced PDCD4 and apoptosis and inhibited cell viability by suppressing miR-21. Furthermore, NVP-LDE-225 inhibited pluripotency-maintaining factors Nanog, Oct-4, c-Myc and Sox-2. The inhibition of Bmi-1 by NVP-LDE-225 was regulated by upregulation of miR-128. NVP-LDE-225 suppressed EMT by upregulating E-cadherin and inhibiting N-cadherin, Snail, Slug and Zeb1 by regulating the miR-200 family. Finally, NVP-LDE-225 inhibited CSC tumor
growth, which was associated with the suppression of Gli1, Gli2, Patched-1, Patched-2, Cyclin D1, Bmi-1 and PCNA and cleavage of caspase-3 and PARP in tumor tissues derived from NOD/SCID IL2Rgamma null mice. Overall, our findings suggest that inhibition of the Shh signaling pathway could therefore be a novel therapeutic option in treating prostate cancer.

[1419]

**TITULO / TITLE:** - Germ-line DICER1 mutations do not make a major contribution to the etiology of familial testicular germ cell tumours.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


[●●Enlace al texto completo (gratuito o de pago) 1186/1756-0500-6-127]

**AUTORES / AUTHORS:** - Sabbaghian N; Bahubeshi A; Shuen AY; Kanetsky PA; Tischkowitz MD; Nathanson KL; Foulkes WD

**INSTITUCIÓN / INSTITUTION:** - Program in Cancer Genetics, Department of Oncology and Human Genetics, McGill University, Montreal, QC, Canada. william.foulkes@mcgill.ca.

**RESUMEN / SUMMARY:** - BACKGROUND: The RNase III enzyme DICER1 plays a central role in maturation of microRNAs. Identification of neoplasia-associated germ-line and somatic mutations in DICER1 indicates that mis-expression of miRNAs in cancer may result from defects in their processing. As part of a recent study of DICER1 RNase III domains in 96 testicular germ cell tumors, a single RNase IIIb domain mutation was identified in a seminoma. To further explore the importance of DICER1 mutations in the etiology of testicular germ cell tumors (TGCT), we studied germ-line DNA samples from 43 probands diagnosed with familial TGCT. FINDINGS: We carried out High Resolution Melting Curve Analysis of DICER1 exons 2-12, 14-19, 21 and 24-27. All questionable melt curves were subjected to confirmatory Sanger sequencing. Sanger sequencing was used for exons 13, 20, 22 and 23. Intron-exon boundaries were included in all analyses. We identified 12 previously reported single nucleotide polymorphisms and two novel single nucleotide variants. No likely deleterious variants were identified; notably no mutations that were predicted to truncate the protein were identified. CONCLUSIONS: Taken together with previous studies, the findings reported here suggest a very limited role for either germ-line or somatic DICER1 mutations in the etiology of TGCT.

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[1420]

**TITULO / TITLE:** - Mannose-sensitive hemagglutinin inhibits proliferation and induces apoptosis in a caspase-dependent manner in human bladder cancer cell lines.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

El objetivo del presente estudio fue investigar los efectos de Pseudomonas aeruginosa mannose-sensitive hemagglutinin (PA-MSHA) en la inhibición del crecimiento de las líneas celulares de cáncer de vejiga y determinar sus mecanismos funcionales. Las células T24 y 5637 fueron tratadas con diferentes concentraciones y tiempos de PA-MSHA. El crecimiento celular fue analizado utilizando el ensayo de CCK-8. La distribución del ciclo celular y la apoptosis inducidas por PA-MSHA se midieron mediante citometría de flujo con propidio iodado (PI) y estandarización FITC con annexin V. La expresión de la apoptosis y los niveles de proteínas del eje PI3K-AKT-mTOR se evaluaron mediante Western blotting. Se observó un efecto tóxico dependiente del tiempo y la concentración de PA-MSHA en las células T24 y 5637. La citometría de flujo con PI y annexin V-FITC mostró que las diferentes concentraciones de PA-MSHA eran capaces de inducir apoptosis y arresto G0-G1 del ciclo celular de las células de cáncer de vejiga. Los niveles de caspasa-8 y caspasa-9 y Fas protein expresiones estaban fuertemente asociados con un aumento en la apoptosis de las células de cáncer de vejiga. Las células estimuladas con PA-MSHA también mostraron una disminución del eje PI3K-AKT-mTOR. PA-MSHA inhibe el crecimiento y induce apoptosis en las líneas celulares de cáncer de vejiga por modulación de la familia de proteínas caspasa y afectando el mecanismo de regulación del ciclo celular. El eje PI3K-AKT-mTOR puede ser importante en el efecto anticáncer fármaco de PA-MSHA.
watsonii) plant extracts in human prostate adenocarcinoma. The cancer ten-
pathway reporter array was performed and revealed that the expression of six
pathway reporters were significantly decreased (Wnt, NFkappaB, Myc/Max,
hypoxia, MAPK/ERK, and MAPK/JNK) in PC-3 cells after treatment with
Phyllanthus extracts. Western blot was conducted and identified several
signalling molecules that were affected in the signalling pathways including pan-
Ras, c-Raf, RSK, Elk1, c-Jun, JNK1/2, p38 MAPK, c-myc, DSH, beta-catenin,
Akt, HIF-1alpha, GSK3beta, NFkappaB p50 and p52, Bcl-2, Bax, and VEGF, in
treated PC-3 cells. A proteomics-based approach, 2D gel electrophoresis, was
performed, and mass spectrometry (MS/MS) results revealed that there were 72
differentially expressed proteins identified in treated PC-3 cells and were
involved in tumour cell adhesion, apoptosis, glycogenesis and glycolysis,
metastasis, angiogenesis, and protein synthesis and energy metabolism.
Overall, these findings suggest that Phyllanthus can interfere with multiple
signalling cascades involved in tumorigenesis and be used as a potential
therapeutic candidate for treatment of cancer.

[1422]
TÍTULO / TITLE: - Prostate cancer: To EBRT or not to EBRT: Surgery or
radiotherapy for localized prostate cancer? That is the question.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
10.1038/nrurol.2013.109.
●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.109
AUTORES / AUTHORS: - Fenner A

[1423]
TÍTULO / TITLE: - Development and validation of a microRNA-based diagnostic
assay for classification of renal cell carcinomas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago)
1016/j.molonc.2013.03.002
AUTORES / AUTHORS: - Spector Y; Fridman E; Rosenwald S; Zilber S; Huang Y;
Barshack I; Zion O; Mitchell H; Sanden M; Meiri E
INSTITUCIÓN / INSTITUTION: - Rosetta Genomics Ltd., Rehovot, Israel.
RESUMEN / SUMMARY: - Renal cancers account for more than 3% of adult
malignancies and cause more than 13,000 deaths per year in the US alone.
The four most common types of kidney tumors include the malignant renal cell
carcinomas; clear cell, papillary, chromophobe and the benign oncocytoma.
These histological subtypes vary in their clinical course and prognosis, and
different clinical strategies have been developed for their management. In some
kidney tumor cases it can be very difficult for the pathologist to distinguish between tumor types on the basis of morphology and immunohistochemistry (IHC). In this publication we present the development and validation of a microRNA-based assay for classifying primary kidney tumors. The assay, which classifies the four main kidney tumor types, was developed based on the expression of a set of 24 microRNAs. A validation set of 201 independent samples was classified using the assay and analyzed blindly. The assay produced results for 92% of the samples with an accuracy of 95%.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
●● Enlace al texto completo (gratuito o de pago) 5489/cuaj.234
AUTORES / AUTHORS: Pruthi DK; Nugent Z; Czaykowski P; Demers AA
INSTITUCIÓN / INSTITUTION: Department of Urology, University of Manitoba, Winnipeg, MB; Department of Epidemiology and Cancer Registry, CancerCare Manitoba, Winnipeg, MB;
RESUMEN / SUMMARY: PURPOSE: We examine the likelihood of a second primary malignancy diagnosis following the diagnosis of urothelial cancer. METHODS: We identified subjects from the Manitoba Cancer Registry diagnosed with urothelial cancer between April 1, 1985 and December 31, 2007. Data were collected on all subsequent new cancer diagnoses. Standardized incidence ratios (SIRs) were calculated for each major cancer type, matched with the general population by age, sex and period. Further analysis was undertaken stratifying by morphology and invasiveness. The results in males were examined with and without prostate cancer. A competing risk model was used to analyze the data controlling for death. RESULTS: Of the 4412 included urothelial cancer cases, 712 patients (16.1%) subsequently developed a second primary malignancy. Risks were highest within 1 year of diagnosis persisting for 5 years. This risk was highest in males aged less than 70 (SIR = 6.25; 95% Confidence Interval [CI] 5.08-7.04). Overall, the risk was similar between the sexes (female SIR: 1.30, CI 1.09-1.54; males 1.42, CI 1.31-1.54; males excluding prostate SIR: 1.22 CI 1.11-1.35). There was an increased relative risk for developing a second primary for cancers of the kidney (male), lung, breast (female) and prostate. Papillary cancers were associated with increased relative risk of developing lung, prostate, and breast (female and male) cancer. In the competing risks model, patients diagnosed with a papillary or in situ urothelial cancer were more likely to be diagnosed with a second primary than non-papillary and invasive disease, respectively. CONCLUSIONS: Those diagnosed with urothelial cancer have an increased probability of having
a second primary cancer detected within the subsequent 5 years, even when prostate cancer is excluded. Papillary tumours in particular may provide a warning for subsequent malignancy.

[1425]

TÍTULO / TITLE: - Diagnosis and management of BHD-associated kidney cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Stamatakis L; Metwalli AR; Middelton LA; Marston Linehan W
INSTITUCIÓN / INSTITUTION: - Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, 10 Center Drive MSC 1107, CRC Room 1W-5940, Bethesda, MD, 20892-1107, USA.

RESUMEN / SUMMARY: - In addition to the associated cutaneous and pulmonary manifestations, individuals with the Birt-Hogg-Dube (BHD) syndrome have an increased risk of developing kidney cancer, which is often bilateral and multifocal. The risk of developing a renal tumor in this population does not decrease with age and therefore warrants a lifelong screening approach. We recommend abdominal imaging every 36 months in individuals without renal lesions at initial screening. Once renal tumors are identified, they should be followed with interval imaging studies until the largest tumor reaches 3 cm in maximal diameter, at which point nephron-sparing surgery should be ideally pursued. While the histology of renal tumors can vary in the BHD syndrome, most tumors possess a relatively indolent natural history and do not require adjuvant therapy if resected when localized to the kidney. With this approach, the vast majority of patients will achieve a curative oncologic outcome and avoid the medical sequelae of chronic renal insufficiency that could otherwise result from total nephrectomy.

[1426]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Makkar M; Dayal P; Gupta C; Mahajan N
INSTITUCIÓN / INSTITUTION: - Department of Pathology, MMISR, Mullana, Ambala, Haryana, India.
RESUMEN / SUMMARY: - Adenomatoid tumor is a benign neoplasm of the male and female genital tracts arising from mesothelial cells. Fine needle aspiration cytology (FNAC) plays a pivotal role in its preoperative diagnosis. Therefore, it
is imperative that pathologists should be well aware of its cytological features so as to avoid erroneous diagnosis and hence prevent unnecessary surgical interventions. We hereby, present a case of adenomatoid tumor of testis in a 41 year male diagnosed by FNAC and later confirmed by histopathological examination.

[1427]

**TÍTULO / TITLE:** - Germline BAP1 mutation predisposes to familial clear-cell renal cell carcinoma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Mol Cancer Res. 2013 May 24.

- Enlace al texto completo (gratis o de pago) 1158/1541-7786.MCR-13-0111

**AUTORES / AUTHORS:** - Farley MN; Schmidt LS; Mester JL; Pena-Llopis S; Pavia-Jimenez A; Christie A; Vocke CD; Ricketts CJ; Peterson J; Middelton L; Kinch L; Grishin N; Merino MJ; Metwalli AR; Xing C; Xie XJ; Dahia PL; Eng C; Linehan WM; Brugarolas J

**INSTITUCIÓN / INSTITUTION:** - University of Texas Southwestern Medical Center.

**RESUMEN / SUMMARY:** - Renal cell carcinoma (RCC) clusters in some families. Familial RCC arises from mutations in several genes, including VHL, which is also mutated in sporadic RCC. However, a significant percentage of familial RCC remains unexplained. Recently, we discovered that the BAP1 gene is mutated in sporadic RCC. BAP1, which encodes a nuclear deubiquitinase, is a two-hit tumor suppressor gene. Somatic BAP1 mutations are associated with high-grade ccRCC and poor patient outcomes. To determine whether BAP1 predisposes to familial RCC, we sequenced the BAP1 gene in 83 unrelated probands with unexplained familial RCC. We identified a novel variant (c.41T>A; p.L14H), which cosegregated with the RCC phenotype. The p.L14H variant targets a highly conserved residue in the catalytic domain, a domain frequently targeted by missense mutations. The family with the BAP1 variant was characterized by early-onset clear cell RCC, occasionally of high Fuhrman grade, and lacked other features that characterize von Hippel-Lindau syndrome. These findings suggest that BAP1 is a familial RCC predisposing gene.

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[1428]

**TÍTULO / TITLE:** - Mutations in LRRC50 predispose zebrafish and humans to seminomas.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


- Enlace al texto completo (gratis o de pago) 1371/journal.pgen.1003384
AUTORES / AUTHORS: Basten SG; Davis EE; Gillis AJ; van Rooijen E; Stoop H; Babala N; Logister I; Heath ZG; Jonges TN; Katsanis N; Voest EE; van Eeden FJ; Medema RH; Ketting RF; Schulte-Merker S; Looijenga LH; Giles RH

INSTITUCIÓN / INSTITUTION: Department of Medical Oncology, University Medical Center Utrecht, Utrecht, The Netherlands.

RESUMEN / SUMMARY: Seminoma is a subclass of human testicular germ cell tumors (TGCT), the most frequently observed cancer in young men with a rising incidence. Here we describe the identification of a novel gene predisposing specifically to seminoma formation in a vertebrate model organism. Zebrafish carrying a heterozygous nonsense mutation in Leucine-Rich Repeat Containing protein 50 (lrrc50 also called dnaaf1), associated previously with ciliary function, are found to be highly susceptible to the formation of seminomas. Genotyping of these zebrafish tumors shows loss of heterozygosity (LOH) of the wild-type lrrc50 allele in 44.4% of tumor samples, correlating with tumor progression. In humans we identified heterozygous germline LRRC50 mutations in two different pedigrees with a family history of seminomas, resulting in a nonsense Arg488* change and a missense Thr590Met change, which show reduced expression of the wild-type allele in seminomas. Zebrafish in vivo complementation studies indicate the Thr590Met to be a loss-of-function mutation. Moreover, we show that a pathogenic Gln307Glu change is significantly enriched in individuals with seminoma tumors (13% of our cohort). Together, our study introduces an animal model for seminoma and suggests LRRC50 to be a novel tumor suppressor implicated in human seminoma pathogenesis.

[1429]

TÍTULO / TITLE: Prostate Cancer Screening in BRCA and Lynch Syndrome Mutation Carriers.

RESUMEN / SUMMARY: Prostate cancer (PrCa) remains a major public health burden worldwide. Screening programs have been established using the most efficient biomarker to date-prostate-specific antigen (PSA)-with the goal of earlier detection of this disease, which is thought to translate to a reduction in
PrCa mortality. However, these screening programs have proved to be controversial following the publication of the two large, randomized, population-based studies in the United States and Europe. There is a recognized need for more refined screening strategies to address some of the deficiencies highlighted in these trials, which include the overdiagnosis and overtreatment of clinically indolent disease. One such strategy could be to include inherited genetic variants in population risk stratification to identify those at higher risk who might benefit more from screening. The genetic component for PrCa risk has been documented from case control and twin studies. The genetic variants include common variants discovered by genome-wide association studies (GWAS). However, their clinical application-including their utility in screening programs-is as yet undefined. There are, however, moderate to rare genetic variants, which confer a much higher risk of PrCa (e.g., BRCA1/2 and mismatch repair [MMR] repair genes). There is more research evidence on the clinical effect of germ-line mutations in these genes; mutation carriers are more likely to develop aggressive PrCa with worse survival. A targeted screening approach might be beneficial if earlier diagnosis, and hence treatment, was to translate into improved outcomes. Clinical trials are currently underway to investigate this further.

[1430]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1155/2013/247504
AUTORES / AUTHORS: - Vicinanza R; Zhang Y; Henning SM; Heber D
INSTITUCIÓN / INSTITUTION: - UCLA Center for Human Nutrition, David Geffen School of Medicine, University of California, Warren Hall, 900 Veteran Avenue 1-2-213, Los Angeles, CA 90095-1742, USA.
RESUMEN / SUMMARY: - Ellagitannins (ETs) from pomegranate juice (PJ) are bioactive polyphenols with chemopreventive potential against prostate cancer (PCa). ETs are not absorbed intact but are partially hydrolyzed in the gut to ellagic acid (EA). Colonic microflora can convert EA to urolithin A (UA), and EA and UA enter the circulation after PJ consumption. Here, we studied the effects of EA and UA on cell proliferation, cell cycle, and apoptosis in DU-145 and PC-3 androgen-independent PCa cells and whether combinations of EA and UA affected cell proliferation. EA demonstrated greater dose-dependent antiproliferative effects in both cell lines compared to UA. EA induced cell cycle arrest in S phase associated with decreased cyclin B1 and cyclin D1 levels. UA induced a G2/M arrest and increased cyclin B1 and cdc2 phosphorylation at
tyrosine-15, suggesting inactivation of the cyclin B1/cdc2 kinase complex. EA induced apoptosis in both cell lines, while UA had a less pronounced proapoptotic effect only in DU-145. Cotreatment with low concentrations of EA and UA dramatically decreased cell proliferation, exhibiting synergism in PC-3 cells evaluated by isobolographic analysis and combination index. These data provide information on pomegranate metabolites for the prevention of PCa recurrence, supporting the role of gut flora-derived metabolites for cancer prevention.

[1431]

**TÍTULO / TITLE:** DNA methylation-based biomarkers in bladder cancer.

**RESUMEN / SUMMARY:** Urinary bladder cancer is the fifth most common cancer in the Western world. Increasing evidence has shown that DNA methylation in bladder cancer is expansive and is implicated in pathogenesis. Furthermore, distinct methylation patterns have been identified between non-muscle-invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC), as well as between FGFR3-mutant and wild-type tumours. Given these distinctions in expression, methylated genes have been proposed as diagnostic and prognostic biomarkers for patients with bladder cancer. Indeed, several studies have revealed that methylated genes including CDH1, FHIT, LAMC2, RASSF1A, TIMP3, SFRP1, SOX9, PMF1 and RUNX3-are associated with poor survival in patients with MIBC. Further validation of these markers for prognostication as well as surveillance (of patients with NMIBC) is required. Validated markers for progression, diagnosis, survival and BCG response will contribute to clinical decision-making and individualized treatment.

[1432]

**TÍTULO / TITLE:** Radio-frequency ablation helps preserve nephrons in salvage of failed microwave ablation for a renal cancer in a solitary kidney.

**RESUMEN / SUMMARY:** Of failed microwave ablation for a renal cancer in a solitary kidney.
Recurrent tumors after renal ablative therapy present a challenge for clinicians. New ablative modalities, including microwave ablation (MWA), have very limited experience in methods of retreating ablation failures. Additionally, in MWA, no long-term outcomes have been reported. In patients having local tumor recurrence, options for surveillance or surgical salvage must be assessed. We present a case to help assess radio-frequency ablation (RFA) for salvage of failed MWA. We report a 63-year-old male with a 4.33-cm renal mass in a solitary kidney undergoing laparoscopic MWA with simultaneous peripheral fiber-optic thermometry (Lumasense, Santa Clara, CA, USA) as primary treatment. Follow-up contrast-enhanced computed tomography (CT) scan was performed at 1 and 4.3 months post-op with failure occurring at 4.3 months as evidenced by persistent enhancement. Subsequently, a laparoscopic RFA (LRFA) with simultaneous peripheral fiber-optic thermometry was performed as salvage therapy. Clinical and radiological follow-up with a contrast-enhanced CT scan at 1 and 11 months post-RFA showed no evidence of disease or enhancement. Creatinine values pre-MWA, post-MWA, and post-RFA were 1.01, 1.14, and 1.17 mg/ml, respectively. This represents a 15% decrease in estimated glomerular filtration rate (eGFR) (79 to 67 ml/min) post-MWA and no change in eGFR post-RFA. Local kidney tumor recurrence often requires additional therapy and a careful decisionmaking process. It is desirable not only to preserve kidney function in patients with a solitary kidney or chronic renal insufficiency, but also to achieve cancer control. We show the feasibility of RFA for salvage treatment of local recurrence of a T1b tumor in a solitary kidney post-MWA.
Several proteins, including seven apolipoproteins, TIM, SAA4, and proEGF were further verified in 111 to 203 individual urine samples from patients with hernia, bladder cancer, or kidney cancer. Six apolipoproteins (APOA1, APOA2, APOB, APOC2, APOC3, and APOE) were able to differentiate bladder cancer from hernia. SAA4 was significantly increased in bladder cancer subgroups, whereas ProEGF was significantly decreased in bladder cancer subgroups. Additionally, the combination of SAA4 and ProEGF exhibited higher diagnostic capacity (AUC=0.80 and p<0.001) in discriminating bladder cancer from hernia than either marker alone. Using MetaCore software to interpret global changes of the urine proteome caused by bladder cancer, we found that the most notable alterations were in immune-response/alternative complement and blood-coagulation pathways. This study confirmed the clinical significance of the urine proteome in the development of non-invasive biomarkers for the detection of bladder cancer. BIOLOGICAL SIGNIFICANCE: In this study, we evaluated the reproducibility of abundant urine protein depletion by hexapeptide-based library beads and an antibody-based affinity column using the iTRAQ technique. The antibody-based affinity-depletion approach, which proved superior, was then applied in conjunction with iTRAQ to discover proteins that were differentially expressed between pooled urine samples from hernia and bladder cancer patients. Several proteins, including seven apolipoproteins, TIM, SAA4, and proEGF were further verified in 111 to 203 individual urine samples from patients with hernia, bladder cancer, or kidney cancer. SAA4 was significantly increased in bladder cancer subgroups, whereas ProEGF was significantly decreased in bladder cancer subgroups. Additionally, the combination of SAA4 and ProEGF exhibited higher diagnostic capacity in discriminating bladder cancer from hernia than either marker alone. A marker panel composed by two novel biomarker candidates, SAA4 and proEGF, was first discovered and verified successfully using Western blotting. To the best of our knowledge, the associations of urinary SAA4 and proEGF with bladder tumor and kidney cancer have not been mentioned before. In the present study, we discovered and verified SAA4 and proEGF as potential bladder cancer biomarker for the first time.

[1434] TITULO / TITLE: - An Alkylphenol Mix Promotes Seminoma Derived Cell Proliferation through an ERalpha36-Mediated Mechanism.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago)
1371/journal.pone.0061758
AUTORES / AUTHORS: - Ajj H; Chesnel A; Pinel S; Plenat F; Flament S; Dumond H
INSTITUCIÓN / INSTITUTION: - CNRS-Universite de Lorraine, UMR 7039, Centre de Recherches en Automatique de Nancy, Vandoeuvre les Nancy, France.
RESUMEN / SUMMARY: - Long chain alkylphenols are man-made compounds still present in industrial and agricultural processes. Their main use is domestic and they are widespread in household products, cleansers and cosmetics, leading to a global environmental and human contamination. These molecules are known to exert estrogen-like activities through binding to classical estrogen receptors. In vitro, they can also interact with the G-protein coupled estrogen receptor. Testicular germ cell tumor etiology and progression are proposed to be stimulated by lifelong estrogen-mimetic exposure. We studied the transduction signaling pathways through which an alkylphenol mixture triggers testicular cancer cell proliferation in vitro and in vivo. Proliferation assays were monitored after exposure to a realistic mixture of 4-tet-octylphenol and 4-nonylphenol of either TCam-2 seminoma derived cells, NT2/D1 embryonal carcinoma cells or testis tumor in xenografted nude mice. Specific pharmacological inhibitors and gene-silencing strategies were used in TCam-2 cells in order to demonstrate that the alkylphenol mix triggers CREB-phosphorylation through a rapid, ERalpha36-PI3kinase non genomic pathway. Microarray analysis of the mixture target genes revealed that this pathway can modulate the expression of the DNA-methyltransferase-3 (Dnmt3) gene family which is involved in DNA methylation control. Our results highlight a key role for ERalpha36 in alkylphenol non genomic signaling in testicular germ cell tumors. Hence, ERalpha36-dependent control of the epigenetic status opens the way for the understanding of the link between endocrine disruptor exposure and the burden of hormone sensitive cancers.

[1435]
TÍTULO / TITLE: - Prostate cancer: Could an antimalarial drug delay the onset of CRPC?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Clyne M

[1436]
TÍTULO / TITLE: - Prevalence of Benign Prostatic Hyperplasia on Jeju Island: Analysis from a Cross-sectional Community-based Survey.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Huh JS; Kim YJ; Kim SD
Institution / Institution: - Department of Urology, Jeju National University School of Medicine, Jeju, Korea.

Resumen / Summary: - Purpose: We report on the prevalence of benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) among men of Jeju Island, representing a coastal and insular area, using a cross-sectional community-based survey. Materials and Methods: A total of 553 participants in a prostate health screening campaign on Jeju Island were subjected to measurements of the International Prostate Symptom Score (IPSS), prostate volume, uroflowmetry, postvoiding residual urine volume, and prostate-specific antigen levels. Eliminating 58 participants who were suspected of having prostate cancer, we analyzed the data from 495 participants. The definition of BPH was a combination of moderate IPSS (8~19) to severe IPSS (>19) and prostate enlargement (>30 g on transrectal ultrasonography).

Results: The prevalence of BPH was 21.0% overall: 11.6% among subjects aged 50~59 years, 18.1% for those aged 60~69, 30.8% for those aged 70~79 and 50.8% among those aged 80 years or more. Compared with previous studies in urban or rural areas, the prevalence was slightly lower. The prevalence of BPH and of moderate to severe LUTS increased with age and showed significant differences between age groups (p=0.028 and 0.033, respectively). A positive correlation was found between the IPSS and quality of life score. Among subunits of IPSS, the nocturia score contributed most to the severity of LUTS and had the highest correlation with a quality of life score.

Conclusions: The overall prevalence of BPH in this study was 21.0%, which is slightly lower than in previous studies in urban or rural areas.

[1437]

Título / Title: - Prima-1 induces apoptosis in bladder cancer cell lines by activating p53.

Resumen / Summary: - Enlace al Resumen / Link to its Summary


Autores / Authors: - Piantino CB; Reis ST; Viana NI; Silva IA; Morais DR; Antunes AA; Dip N; Srougi M; Leite KR

Institución / Institution: - Laboratory of Medical Investigation, Urology Department - LIM55, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil.

Resumen / Summary: - Objectives: Bladder cancer represents 3% of all carcinomas in the Brazilian population and ranks second in incidence among urological tumors, after prostate cancer. The loss of p53 function is the main genetic alteration related to the development of high-grade muscle-invasive disease. Prima-1 is a small molecule that restores tumor suppressor function to mutant p53 and induces cancer cell death in various cancer types. Our aim was to investigate the ability of Prima-1 to induce apoptosis after DNA damage in bladder cancer cell lines. Method: The therapeutic effect of Prima-1 was
studied in two bladder cancer cell lines: T24, which is characterized by a p53 mutation, and RT4, which is the wild-type for the p53 gene. Morphological features of apoptosis induced by p53, including mitochondrial membrane potential changes and the expression of thirteen genes involved in apoptosis, were assessed by microscopic observation and quantitative real-time PCR (qRT-PCR). RESULTS: Prima-1 was able to reactivate p53 function in the T24 (p53 mt) bladder cancer cell line and promote apoptosis via the induction of Bax and Puma expression, activation of the caspase cascade and disruption of the mitochondrial membrane in a BAK-independent manner. CONCLUSION: Prima-1 is able to restore the transcriptional activity of p53. Experimental studies in vivo may be conducted to test this molecule as a new therapeutic agent for urothelial carcinomas of the bladder, which characteristically harbor p53 mutations.

1036

[1438]
TÍTULO / TITLE: - Oncomir miR-125b suppresses p14(ARF) to modulate p53-dependent and p53-independent apoptosis in prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago)
1371/journal.pone.0061064
AUTORES / AUTHORS: - Amir S; Ma AH; Shi XB; Xue L; Kung HJ; Devere White RW
INSTITUCIÓN / INSTITUTION: - Department of Urology, University of California Davis, Sacramento, California, United States of America.
RESUMEN / SUMMARY: - MicroRNAs are a class of naturally occurring small non-coding RNAs that target protein-coding mRNAs at the post-transcriptional level and regulate complex patterns of gene expression. Our previous studies demonstrated that in human prostate cancer the miRNA miR-125b is highly expressed, leading to a negative regulation of some tumor suppressor genes. In this study, we further extend our studies by showing that miR-125b represses the protein product of the ink4a/ARF locus, p14(ARF), in two prostate cancer cell lines, LNCaP (wild type-p53) and 22Rv1 (both wild type and mutant p53), as well as in the PC-346C prostate cancer xenograft model that lentivirally overexpressed miR-125b. Our results highlight that miR-125b modulates the p53 network by hindering the down-regulation of Mdm2, thereby affecting p53 and its target genes p21 and Puma to a degree sufficient to inhibit apoptosis. Conversely, treatment of prostate cancer cells with an inhibitor of miR-125b (anti-miR-125b) resulted in increased expression of p14(ARF), decreased level of Mdm2, and induction of apoptosis. In addition, overexpression of miR-125b in p53-deficient PC3 cells induced down-regulation of p14(ARF), which leads to increased cell proliferation through a p53-independent manner. Thus, we
conclude that miR-125b acts as an oncogene which regulates p14(ARF)/Mdm2 signaling, stimulating proliferation of prostate cancer cells through a p53-dependent or p53-independent function. This reinforces our belief that miR-125b has potential as a therapeutic target for the management of patients with metastatic prostate cancer.

[1439]

TÍTULO / TITLE: - Deletion of p21/Cdkn1a confers protective effect against prostate tumorigenesis in transgenic adenocarcinoma of the mouse prostate model.


AUTORES / AUTHORS: - Jain AK; Raina K; Agarwal R

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical Sciences; Skaggs School of Pharmacy and Pharmaceutical Sciences; University of Colorado Anschutz Medical Campus; Aurora, CO USA.

RESUMEN / SUMMARY: - Cyclin-dependent kinase inhibitors (CDKIs) p21 (Cip1/Waf1) (p21) and p27 (Kip1) (p27) play a determining role in cell cycle progression by regulating CDK activity; however, p21 role in prostate cancer (PCa) is controversial. Whereas p21 upregulation by anticancer agents causes cell cycle arrest in various PCa cell lines, elevated p21 levels have been associated with higher Gleason score, poor survival and increased PCa recurrence. These conflicting findings suggest that more studies are needed to examine p21 role in PCa. Herein, employing genetic approach, transgenic mice harboring p21/Cdkn1a homozygous deletion (p21 (-/-) ) were crossed with the transgenic adenocarcinoma of the mouse prostate (TRAMP) mice to characterize in vivo consequences of p21 deletion on prostate tumorigenesis. Lower urogenital tract weight of p21 (-/-) /TRAMP mice was significantly lower than those of p21 (+/-) /TRAMP and TRAMP mice. Histopathology further supported these observations, showing less aggressiveness in prostates of p21 (-/-) /TRAMP. Furthermore, a significantly higher incidence of low-grade prostatic intraepithelial lesions (PIN) with a concomitant reduction in adenocarcinoma incidence was observed in p21 (-/-) /TRAMP mice compared with TRAMP mice. In addition, whereas TRAMP mice showed the presence of poorly differentiated adenocarcinoma lesions, no such lesions were observed in p21/TRAMP transgenic mice. Specifically, there was a significant reduction in the severity of lesions in both p21 (-/-) /TRAMP and p21 (+/-) /TRAMP mice compared with TRAMP mice. Together, our data showed that p21 deletion reduces prostate tumorigenesis by slowing-down progression of PIN (pre-malignant) to adenocarcinoma (malignant), suggesting that intact p21

1037
expression is associated with PCa aggressiveness, while its decreased levels may in fact confer protection against prostate tumorigenesis.

[1440]

TÍTULO / TITLE: - Surgical management of a locally advanced symptomatic recurrence of penile sarcoma secondary to prostate brachytherapy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Hakky TS; Espiritu P; Rodriguez AR; Gould N; Spiess PE

INSTITUCIÓN / INSTITUTION: - Department of Genitourinary Oncology, Moffitt Cancer Center and Department of Urology, University of South Florida, Tampa, Florida, USA.

RESUMEN / SUMMARY: - Background: The surgical management of patients with symptomatic metastatic or locally advanced recurrences involving the penis remains poorly characterized. The aim of the present abstract and video is to detail our experience in the surgical management of a specific patient with a locally advanced symptomatic recurrence of penile sarcoma secondary to prostate cancer treated with primary brachytherapy. Materials and Methods: A 70 year old male patient initially treated for localized prostate cancer with interstitial brachytherapy at an outside facility developed an unfortunate secondary malignancy consisting of a locally advanced penile sarcoma involving as well the prostate and base of the bladder. Despite our best efforts to control his pain, he developed a very symptomatic local recurrence with a secondary penile abscess and purulent periurethral drainage. At this time, it was felt a surgical resection consisting of a total penectomy, urethrectomy, cystoprostatectomy, and ileal conduit urinary diversion would be the best option for local cancer control in this particular patient. Results: The patient underwent the surgical resection without any complications as illustrated in this surgical video, with a jejunal intestinal mass identified at the time of surgery which was resected with a primary bowel anastomosis performed. The patient was discharged from hospital uneventfully with his symptomatic local recurrence being successfully managed and the patient no longer requiring oral narcotics for pain control. The pathological report confirmed a locally advanced sarcoma involving the penile, prostate, and bladder which was resected with negative surgical margins and the jejunal mass was confirmed to represent a small bowel sarcoma metastatic site. Conclusion: As highlighted in the present video, the treatment of a symptomatic sarcoma local recurrence contiguously involving the penis can be successfully managed provided the patient is informed of the potential morbidity and psychosocial implications imparted by performing a total penectomy and adjacent organ resection.

1038
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Weng CS; Chen MY; Wang TY; Tsai HW; Hung YC; Yu KJ; Chiang YC; Lin H; Lu CH; Chou HH
INSTITUCIÓN / INSTITUTION: - Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan.

RESUMEN / SUMMARY: - OBJECTIVE: To report the natural history and prognosis of the uncommon Sertoli-Leydig cell tumor (SLCT) of the ovary. MATERIALS AND METHODS: A 20-year retrospective review was conducted by the Taiwanese Gynecologic Oncology Group (TGOG), including nine tertiary medical centers from different regions in Taiwan. The medical records for 40 cases of ovarian SLCT were collected. Pathology reviews were carried out by a panel of expert pathologists. RESULTS: After pathological review, 17 patients were subsequently excluded because the pathology slides were unavailable in five cases, and discrepant results from the initial diagnosis were found in 12 cases (34%). For the remaining 23 patients, the median age was 41 years. The most common symptom was irregular vaginal bleeding followed by an abdominal mass or amenorrhea. Most of the tumors were unilateral and confined to the right ovary, with an average size of 8.2 cm. Preoperative serum markers were available for 12 patients and were elevated for three patients. All patients underwent primary surgery. Six patients accepted adjuvant chemotherapy, and bleomycin, etoposide, and cisplatin were used in four of them. Clinical follow-up information was available in 21 patients with a median of 19 months. Eighty-two percent of patients were alive and free of disease up to the date of the last follow-up. Two patients died of the disease. CONCLUSION: This study demonstrates the extreme rarity of ovarian SLCT in Taiwan. Histological discordance between the diagnosis and central review proves the need for expertise review before treatment. For an improved understanding of the biological behavior and treatment strategy for this unique tumor, international collaboration is imperative.

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TÍTULO / TITLE: - Metabolic and toxicological considerations of newly approved prostate cancer drugs.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

1517/17425255.2013.789019
INTRODUCCIÓN / SUMMARY: - Introduction: Despite increasing early detection and treatment of prostate cancer, a subset of patients presents with or develops metastatic disease. Androgen deprivation therapy is effective but resistance eventually develops, resulting in a lethal phenotype known as castration-resistant prostate cancer (CRPC). Recently, several novel treatments, each with distinct mechanisms of actions, have been approved for the treatment of CRPC. Understanding of the metabolic and toxicological considerations of each treatment is crucial to the successful management of patients with this lethal disease. Areas covered: The present review focuses on the metabolism and toxicology characteristics of recently approved therapies in the treatment of metastatic CRPC. Specifically, the authors review the mechanism of action of these therapies in addition to their efficacy and usage recommendations for hepatic and renal impairment. The authors, furthermore, also consider their adverse effect profile. Expert opinion: Despite the expanding armamentarium of effective treatments for CRPC, the exact choice, timing and sequence of various therapies remains an inexact science and requires further investigation. Variations in patient comorbidities, disease burden, organ functions and adverse events are all critical determinants in selection of treatment. Identification and validation of molecular pathways and specific targets that drives disease progression will be critical in the continued development of effective treatments in advanced prostate cancer.

[1443]

TÍTULO / TITLE: - Neonatal sacrococcygeal teratoma with acute renal failure.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ahmad M; Arora M; Ullah E; Malik AM

INSTITUCIÓN / INSTITUTION: - Department of Radiodiagnosis, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India.

RESUMEN / SUMMARY: - Teratomas are germ cell tumours composed of multiple types of cells derived from more than a single germ cell layer. The most common site of an extragonadal teratoma is the sacrococcygeal region. We report a case of a 16-day-old female child with a large swelling in the
sacroccocygeal region extending laterally into the buttocks with severely deranged renal functions. Ultrasonography and CT helped in making the diagnosis and, more importantly, to delineate the extent of the tumour and the involvement of adjacent organs and tissues: in our case, lower bilateral ureters. Imaging findings and clinical presentation led to the diagnosis of sacrococcygeal teratoma with renal failure.

[1444]

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Kim J; Yu HS; Cho KS; Han WK; Ham WS
INSTITUCIÓN / INSTITUTION: Department of Urology, Urological Science Institute, Yonsei University College of Medicine, Seoul, Korea.
RESUMEN / SUMMARY: PURPOSE: The proper indication for laparoendoscopic single-site surgery (LESS) in urology is still under debate, especially for malignant diseases. We compared the perioperative outcomes between LESS and conventional laparoscopy (CL) for upper urinary tract malignancies.
MATERIALS AND METHODS: We reviewed the records of 75 patients who underwent radical nephrectomy, nephroureterectomy with bladder cuff excision, or partial nephrectomy with the LESS or CL approach between December 2008 and December 2010. We compared characteristics and perioperative outcomes between patients who underwent LESS or CL. All operations were performed by three surgeons using the transperitoneal approach. RESULTS: For all three surgery types, no differences in patient characteristics, estimated blood losses, transfusion rates, or durations of hospital stay were found between the two groups. No complications were found between the two groups in those who underwent nephroureterectomy; however, significantly more complications were found in the LESS group than in the CL group in those who underwent radical nephrectomy or partial nephrectomy. Most of the complications with LESS radical nephrectomy occurred in the early introduction period of the technique. CONCLUSIONS: No significant differences in perioperative outcomes were found between the LESS and CL groups in those who underwent radical nephrectomy or nephroureterectomy with bladder cuff excision. Therefore, the use of LESS in these cases is expected to expand as surgeons gain more experience with this technique and as other technical advances in laparoscopic instruments occur. However, partial nephrectomy with LESS should be performed restrictively considering the current level of surgical skill.
Small renal masses: surgery or surveillance.

TÍTULO / TITLE: - Small renal masses: surgery or surveillance.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hwang EC; Yu HS; Kwon DD
INSTITUCIÓN / INSTITUTION: - Department of Urology, Chonnam National University Medical School, Gwangju, Korea.
RESUMEN / SUMMARY: - The incidence of kidney cancer has been rising over the past two decades, especially in cases in which the disease is localized and small in size (<4 cm). This rise is mainly due to the widespread use of routine abdominal imaging such as ultrasonography, computed tomography, and magnetic resonance imaging. Early detection was initially heralded as an opportunity to cure an otherwise lethal disease. However, despite increasing rates of renal surgery in parallel to this trend, mortality rates from renal cell carcinoma have remained relatively unchanged. Moreover, data suggest that a substantial proportion of small renal masses are benign. As a result, the management of small renal masses has continued to evolve along two basic themes: it has become less radical and less invasive. These shifts are in part a reflection of an improved understanding that the biology of incidentally discovered renal cell carcinoma may be more indolent than previously thought. However, not all small renal masses are indolent, and de novo metastatic disease can develop at the initial presentation. Therefore, it is with this background of clinical uncertainty and biological heterogeneity that clinicians must interpret the benefits and disadvantages of various clinical approaches to small renal masses.

Enhanced delivery system of flutamide loaded chitosan-dextran sulphate nanoparticles for prostate cancer.

TÍTULO / TITLE: - Enhanced delivery system of flutamide loaded chitosan-dextran sulphate nanoparticles for prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Anitha A; Uthaman S; Nair SV; Jayakumar R; Lakshmanan VK
INSTITUCIÓN / INSTITUTION: - Amrita Centre for Nanosciences and Molecular Medicine, Amrita Institute of Medical Sciences and Research Centre, Amrita Vishwa Vidyapeetham, Kochi 682041, Kerala, India.
RESUMEN / SUMMARY: - In the current work, a sustained drug delivery system of flutamide (FLT) was developed using chitosan (CS) and dextran sulphate (DS) nanoparticles and were characterized using different techniques. The prepared nanoparticles showed a size of 80-120 nm with an entrapment efficiency of 55 +/- 6.95%. In addition, blood compatibility, in vitro cytotoxicity, drug release and
cellular uptake studies were also carried out. The drug release studies showed a sustained and pH dependent release pattern as a result, after 120 h about 66% drug release occurred at pH 7.4 and 78% release occurred in acidic pH. MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) and LDH (lactate dehydrogenase) experiments proved the preferential toxicity of drug loaded nanoparticles towards prostate cancer cells (PC3) unlike in normal cells, mouse fibroblast cells (L929). The cell death mechanism of drug loaded nanoparticles for a concentration of 50 and 75 nM showed 28 +/- 2 and 35.2 +/- 4% apoptosis in samples treated with the PC3 cells after 24 h. Fluorescent microscopic imaging and flow cytometry confirmed the preferential uptake of the nanoparticles (NPs) in the prostate cancer cells (PC3) unlike in normal (L929) cells. Hence the developed FLT loaded CS-DS NPs could be used as a promising system for controlled delivery in prostate cancer.

[1447]

**TÍTULO / TITLE:** Safety and efficacy of 120w high performance system greenlight laser vaporization for non-muscle-invasive bladder cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Tao W; Yang D; Shan Y; Xue B; Sun C; Zang Y; Zhang Y

**INSTITUCIÓN / INSTITUTION:** Department of Urology, the Second Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China.

**RESUMEN / SUMMARY:** OBJECTIVE: We evaluated the safety and efficacy of 120W potassium-titanate-phosphate (KTP) laser vaporization on patients with non-muscle invasive bladder cancer compared with standard transurethral resection of bladder tumor (TUR-BT). MATERIALS AND METHODS: One hundred and fifty-eight patients of non-muscle invasive bladder cancer who underwent either 120W potassium-titanate-phosphate (KTP) laser vaporization (HPS group, n=74) or transurethral resection of the bladder tumor (TUR-BT group, n=84) were analyzed respectively. The preoperative, intraoperative and postoperative clinical data were recorded and compared in two groups. RESULTS: All patients were successfully treated with 120W-KTP laser vaporization or TUR-BT. No significant differences were observed in operative time, perioperative and postoperative serum sodium and hemoglobin levels between two groups. Importantly, HPS had less specific side effects of TURBT, such as obturator nerve reflex, postoperative bladder irrigation and catheterization time, which shows statistic difference significantly (p< 0.05). Recurrence rate was lower in HPS group than those in TUR-BT group. CONCLUSION: The 120W-HPS KTP laser as a safe and feasible procedure
provides an alternative for the patients with non-muscle invasive bladder cancer, especially for those on anticoagulation therapy.

[1448]

TÍTULO / TITLE: - Targeting molecular aberrations in urothelial carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Apolo AB; Kwiatkowski DJ
INSTITUCIÓN / INSTITUTION: - From the Medical Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD; the Translational Medicine Division, Brigham and Women’s Hospital, Harvard Medical School, Dana-Farber Cancer Institute, Boston, MA.

RESUMEN / SUMMARY: - Advances in tumor biology and cancer genetics have led to the development of effective targeted therapies in oncology over the past decade. However, targeted drug development for urothelial carcinoma has been slower than for some other malignancies. The path forward in drug development is through a better understanding of the aberrant pathways driving urothelial tumor development. Steady progress has been made in the characterization of genomic alterations in urothelial carcinoma. The Cancer Genome Atlas (TCGA) project is well underway in the analysis of a large set of urothelial cancer specimens using multiple approaches and technologies. In addition, there are already many well-established mutations and genetic alterations in urothelial carcinoma that likely contribute in an important way to tumor development. In addition, urothelial cancer genome-wide association studies have identified common variants associated with urothelial cancer risk and protein expression that can potentially be therapeutically targeted. Furthermore, the MET pathway has emerged as an exciting target in multiple tumors, including urothelial carcinoma. Our knowledge of how to clinically target many emerging molecular aberrations in urothelial cancer is still in the early stages of development. However, there is much promise in the ongoing research being conducted in urothelial cancer molecular pathogenesis.

[1449]

TÍTULO / TITLE: - Comprehensive molecular oncogenomic profiling and miRNA analysis of prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Sethi S; Kong D; Land S; Dyson G; Sakr WA; Sarkar FH
INSTITUCIÓN / INSTITUTION: - Departments of Pathology & Oncology, and division of Statistics, Karmanos Cancer Institute, Wayne State University School of Medicine and Detroit Medical Center Detroit, MI.

RESUMEN / SUMMARY: - This study was focused on molecular profiling of prostate cancer (PCa) using scant amounts of both frozen and formalin-fixed paraffin-embedded (FFPE) PCa tissue specimens. DNA and RNA were extracted and interrogated for: (1) whole-genome gene expression profiling, (2) miRNA expression analysis, (3) SNP analysis, and (4) mutation analysis. Data was statistically analyzed and correlated with clinical and pathologic variables. Expression profiling of 47,224 genes revealed 74 genes that were significant in predicting high tumor grade in PCa (p<0.0001). These were involved in many cellular processes as analyzed by Ingenuity Pathway Analysis (IPA). Using novel high throughput technologies, we identified a specific oncogenicomic and miRNA signatures showing loss of miR-34 expression. Interestingly, p53 was at the center hub of the signaling pathways, and the loss of miR-34 expression was consistent with the central role of p53 in PCa. Analysis of 731,442 SNP’s, revealed 638 SNP’s that were significant in predicting high tumor grade (p<0.0001; logistic regression analysis). We also found, for the first time, a novel hot spot mutation in MET oncogene, variant T992I, suggesting that our findings would be useful in further defining the role of specific regulatory genes and miRNAs in the pathological evolution of PCa, and could also have potential clinical utility in improving diagnostic accuracy, refining prognostic and predictive capabilities and may serve as therapeutic targets.

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TÍTULO / TITLE: - The Interactions of Dietary Tomato Powder and Soy Germ on Prostate Carcinogenesis in the TRAMP Model.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Zuniga KE; Clinton SK; Erdman JW Jr

INSTITUCIÓN / INSTITUTION: - Division of Nutritional Sciences and Department of Food Science and Human Nutrition, University of Illinois at Urbana-Champaign, 905 S. Goodwin Ave, Urbana, IL 61801. jwerdman@illinois.edu.

RESUMEN / SUMMARY: - The interactions between bioactive-rich food components within a complex human diet for the inhibition of prostate carcinogenesis are largely unknown and difficult to quantify in humans. Tomato and soy products have each shown anti-prostate cancer (PCa) activity in laboratory studies. The objective of this study was to determine the efficacy of dietary tomato and soy germ, alone and in combination, for the inhibition of PCa in the transgenic adenocarcinoma of the mouse prostate (TRAMP) model.
At 4 weeks of age, male C57BL/6 x FVB TRAMP mice (n = 119) were randomized to consume: AIN-93G control, 10% whole tomato powder (TP), 2% soy germ powder (SG), or 10% tomato powder with 2% soy germ powder (TP+SG) for 14 weeks. One hundred percent of mice fed the control diet had PCa, whereas PCa incidence was significantly lower in mice consuming TP (61%, P < 0.001), SG (66%, P < 0.001), and TP+SG (45%, P < 0.001).

Although the protection offered by the combination of TP and SG was not synergistic, it was the most effective intervention. TP, SG, and TP+SG increased apoptotic index (AI) and modestly reduced the proliferative index (PI) in the prostate epithelium of TRAMP mice exhibiting primarily prostatic intraepithelial neoplasia. The dramatic reduction in the PI/AI ratio by the dietary interventions suggests that the control mice experience a stronger stimulus for malignant progression in the prostate microenvironment. Maximally effective and safe strategies for PCa prevention may result from optimizing combinations of nutrients and bioactives through an orchestration of dietary patterns. Cancer Prev Res; 6(6); 548-57. ©2013 AACR.

[1451]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Mizuno S; Yamagishi Y; Ebinuma H; Nakamoto N; Katahira M; Sasaki A; Sakamoto M; Suzuki H; Kanai T; Hibi T
INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology and Hepatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, 160-8582 Japan.
RESUMEN / SUMMARY: - A 58-year-old man was diagnosed as a hepatitis B virus (HBV) carrier approximately 30 years ago. He was diagnosed with renal cell carcinoma when he was 57 years old. Radical nephrectomy was performed, and everolimus was administered to treat his lung metastasis. After beginning the everolimus, intermittent fever, general fatigue, and jaundice developed. He was admitted under a diagnosis of flare (acute exacerbation) of chronic B hepatitis due to HBV reactivation. Despite intensive care, he died of hepatic failure and fungus infection. The autopsy findings were compatible with hepatic failure due to HBV reactivation by everolimus. Antiviral prophylaxis must be taken into consideration before beginning immunosuppressive therapy such as everolimus in HBV carriers.

[1452]
CK2-NCoR signaling cascade promotes prostate tumorigenesis.

The aberrant expressions of casein kinase 2 (CK2) was found in prostate cancer patient and cell lines, but little is known of the detailed mechanisms implicated in prostate tumorigenesis. In this study, we report that both CK2 activity and CK2-mediated NCoR phosphorylation are significantly elevated in the androgen-independent prostate cancer cell line DU145 and PC-3 compared with RWPE1 and LNCaP cells. Increased phosphorylation inversely correlates with the mRNA level of the NCoR-regulated gene, interferon-gamma-inducible protein 10 (IP-10). CK2 inhibition abrogated NCoR phosphorylation, IP-10 transcriptional repression, and the invasion activity of PC-3 cells. Inhibition of the CK2-NCoR network significantly reduced in vivo PC-3 cell tumorigenicity, likely due to transcriptional derepression of IP-10. Clinicopathological analyses revealed that increased CK2-mediated NCoR phosphorylation significantly correlates with poor survival among prostate cancer patients. These findings elucidate a CK2-modulated oncogenic cascade in prostate tumorigenesis.

Cancer fatalism is believed to be a major barrier for cancer screening in Black males. Therefore, the purpose of this study was to compare perceptions of prostate cancer (CaP) fatalism and predictors of CaP screening with Prostate Specific Antigen (PSA) testing between U.S.-born and Caribbean-born Black males.
Caribbean-born Black males. The Powe Fatalism Inventory and the Personal Integrative Model of CaP Disparity Survey were used to collect the following data from males in South Florida. Multivariate logistic regression models were constructed to examine the statistically significant predictors of CaP screening. A total of 211 U.S.-born and Caribbean-born Black males between ages 39-75 were recruited. Nativity was not a significant predictor of CaP screening with PSA testing within the last year (Odds ratio [OR] = 0.80, 95 % confidence interval [CI] = 0.26, 2.48, p = 0.70). Overall, higher levels of CaP fatalism were not a significant predictor of CaP screening with PSA testing within the last year (OR = 1.37, 95 % CI = 0.48, 3.91, p = 0.56). The study results suggest that nativity did not influence CaP screening with PSA testing. However, further studies are needed to evaluate the association between CaP screening behavior and levels of CaP fatalism.

[1454]
TÍTULO / TITLE: - Discovering smoking-related pathway alterations in urothelial cell carcinoma pathogenesis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 4161/cc.24852
AUTORES / AUTHORS: - Martignoni G
INSTITUCIÓN / INSTITUTION: - Department of Pathology and Diagnostics; University of Verona; Verona, Italy.

[1455]
TÍTULO / TITLE: - Can we stop ordering prostate-specific antigen screening tests?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JAMA. Acceso gratuito al texto completo.
  ●●Enlace a la Editora de la Revista http://jama.ama-assn.org/search.dtl
  ●●Enlace al texto completo (gratuito o de pago) 1001/jamainternmed.2013.1164
AUTORES / AUTHORS: - Katz MH

[1456]
TÍTULO / TITLE: - Epigenetic mechanisms in penile carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 3390/ijms140610791
Penile carcinoma (PeCa) represents an important public health problem in poor and developing countries. Despite its unpredictable behavior and aggressive treatment, there have only been a few reports regarding its molecular data, especially epigenetic mechanisms. The functional diversity in different cell types is acquired by chromatin modifications, which are established by epigenetic regulatory mechanisms involving DNA methylation, histone acetylation, and miRNAs. Recent evidence indicates that the dysregulation in these processes can result in the development of several diseases, including cancer. Epigenetic alterations, such as the methylation of CpGs islands, may reveal candidates for the development of specific markers for cancer detection, diagnosis and prognosis. There are a few reports on the epigenetic alterations in PeCa, and most of these studies have only focused on alterations in specific genes in a limited number of cases. This review aims to provide an overview of the current knowledge of the epigenetic alterations in PeCa and the promising results in this field. The identification of epigenetically altered genes in PeCa is an important step in understanding the mechanisms involved in this unexplored disease.

[1457]

**TÍTULO / TITLE:** - Multiphase computed tomography of malignant kidney tumors: radiologic-pathologic comparison.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Zokalj I; Marotti M; Saghir H; Gasparov S; Kolaric B; Plesnar A

**INSTITUCIÓN / INSTITUTION:** - Department of Radiology and Ultrasound, Cakovec County Hospital, Cakovec, Croatia. ivan.zokalj@ck.t-com.hr

**RESUMEN / SUMMARY:** - The aim of this retrospective study was to evaluate diagnostic test parameters of multiphase spiral computed tomography (CT) of the kidneys in the assessment of malignant renal tumors. Fifty-one patient records were reviewed. The imaging protocol included unenhanced and postcontrast scans during arterial and nephrographic phase. CT findings were compared with pathology findings to assess the value of spiral CT (sensitivity, specificity, negative predictive value, positive predictive value and accuracy) in the detection and characterization of tumors, and in the evaluation of local extension of malignant renal tumors. Spiral CT had a 96.08% sensitivity and accuracy in the detection of tumors. Characterization of renal tumors with CT had a sensitivity of 94.12% and accuracy of 96.08%. In the detection of fibrous capsule penetration, CT reached a sensitivity of 91.97% and specificity of...
51.28%. In the evaluation of canal system propagation, the sensitivity was 100% and specificity 90.70%. CT had a sensitivity of 75%, specificity of 95.75% and positive predictive value of 60% in the evaluation of regional lymph node involvement. In the detection of the main renal vein invasion, CT showed 60% sensitivity and 100% specificity. Spearman’s rank correlation coefficient between the mean tumor size on CT images and renal specimen was 0.916. In conclusion, multiphase spiral CT has satisfactory diagnostic parameters in the detection, characterization and evaluation of local extension of renal tumors except for detection of the main renal vein invasion.

[1458]
TÍTULO / TITLE: - Kidney cancer: Multiphasic CT to distinguish small renal mass subtype.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Fenner A

[1459]
TÍTULO / TITLE: - The effect of vascular endothelial growth factor in the progression of bladder cancer and diabetic retinopathy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Aldebasi YH; Rahmani AH; Khan AA; Aly SM
INSTITUCIÓN / INSTITUTION: - Department of optometry, College of Applied Medical Sciences, Qassim University Saudi Arabia.
RESUMEN / SUMMARY: - Bladder cancer and diabetic retinopathy is a major public health and economical burden worldwide. Despite its high prevalence, the molecular mechanisms that induce or develop bladder carcinomas and diabetic retinopathy progression are poorly understood but it might be due to the disturbance in balance between angiogenic factors such as VEGF and antiangiogenic factors such as pigment epithelium derived growth factor. VEGF is one of the important survival factors for endothelial cells in the process of normal physiological and abnormal angiogenesis and induce the expression of antiapoptotic proteins in the endothelial cells. It is also the major initiator of angiogenesis in cancer and diabetic retinopathy, where it is up-regulated by oncogenic expression and different type of growth factors. The alteration in VEGF and VEGF receptors gene and overexpression, determines a diseases phenotype and ultimately the patient’s clinical outcome. However, expressional and molecular studies were made on VEGF to understand the exact mechanism of action in the genesis and progression of bladder carcinoma and diabetic retinopathy, but still how VEGF mechanism involve in such type of disease progression are not well defined. Some other factors also play a
significant role in the process of activation of VEGF pathways. Therefore, further detailed analysis via molecular and therapeutic is needed to know the exact mechanisms of VEGF in the angiogenesis pathway. The detection of these types of diseases at an early stage, predict how it will behave and act in response to treatment through regulation of VEGF pathways. The present review aimed to summarize the mechanism of alteration of VEGF gene pathways, which play a vital role in the development and progression of bladder cancer and diabetic retinopathy.

[1460]
**TITULO / TITLE:** Use of a glycolipid inhibitor to ameliorate renal cancer in a mouse model.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago)
**AUTORES / AUTHORS:** Chatterjee S; Alsaeedi N; Hou J; Bandaru VV; Wu L; Halushka MK; Pili R; Ndikuyeze G; Haughey NJ
**INSTITUCIÓN / INSTITUTION:** Department of Pediatrics, Division of Pediatric Cardiology, The Johns Hopkins Medical Institutions, Baltimore, Maryland, United States of America.
**RESUMEN / SUMMARY:** In a xenograft model wherein, live renal cancer cells were implanted under the kidney capsule in mice, revealed a 30-fold increase in tumor volume over a period of 26 days and this was accompanied with a 32-fold increase in the level of lactosylceramide (LacCer). Mice fed D-threo-1-phenyl-2-decanoylamino-3-morpholino-1-propanol (D-PDMP), an inhibitor of glucosylceramide synthase and lactosylceramide synthase (LCS: beta-1,4-GalT-V), showed marked reduction in tumor volume. This was accompanied by a decrease in the mass of lactosylceramide and an increase in glucosylceramide (GlcCer) level. Mechanistic studies revealed that D-PDMP inhibited cell proliferation and angiogenesis by inhibiting p44MAPK, p-AKT-1 pathway and mammalian target for rapamycin (mTOR). By linking glycosphingolipid synthesis with tumor growth, renal cancer progression and regression can be evaluated. Thus inhibiting glycosphingolipid synthesis can be a bonafide target to prevent the progression of other types of cancer.

[1461]
**TITULO / TITLE:** Testicular cancer: Changing patterns of incidence in testicular germ cell tumours.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.79
AUTORES / AUTHORS: - Singhera M; Huddart R
INSTITUCIÓN / INSTITUTION: - Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey SM2 5PT, UK.

[1462]
TÍTULO / TITLE: - Symptomatic bilateral testicular metastasis from carcinoma of the prostate.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace a la Editora de la Revista http://bmj.com/search.dtl
  ●●Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-009008
AUTORES / AUTHORS: - Upchurch EA; Khan F; Okeke A
INSTITUCIÓN / INSTITUTION: - Department of Upper GI Surgery, Gloucestershire Royal Hospital, Cheltenham, UK. em_upchurch@hotmail.com
RESUMEN / SUMMARY: - A man in his late 70s, on hormonal treatment for prostatic adenocarcinoma, presented with bilateral enlarged and painful testes. Bilateral orchidectomy was undertaken and subsequent histological examination revealed both testes completely infiltrated with metastatic prostatic carcinoma.

[1463]
TÍTULO / TITLE: - Primary intratesticular rhabdomyosarcoma in pediatrics.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 4103/0970-1591.109995
AUTORES / AUTHORS: - Nasit JG; Parikh B; Trivedi P; Shah M
INSTITUCIÓN / INSTITUTION: - Department of Pathology, P.D.U. Medical College, Rajkot, Gujarat, India.
RESUMEN / SUMMARY: - Testicular sarcomas constitute only 1-2% of all testicular tumors and are mostly associated with germ cell tumor. Primary intratesticular rhabdomyosarcoma is rare and only 14 cases have been reported in the literature till date. It should be differentiated from germ cell tumor with sarcomatous component, other intratesticular spindle-cell sarcomas and paratesticular rhabdomyosarcoma. Accurate diagnosis and early treatment is essential as it is an aggressive tumor with high metastatic potential and poor prognosis. Orchidectomy is the treatment of choice. Chemo-radiotherapy is recommended in case of recurrence and metastasis.

[1464]
**TÍTULO / TITLE:** Metanephric stromal tumour: A rare pediatric benign stromal specific renal neoplasm.

**RESUMEN / SUMMARY:** A case of incidentally detected Metanephric Stromal Tumour (MST) is reported here. This is a rare, recently recognized pediatric benign stromal specific renal neoplasm. A review of the English literature revealed only five cases after its original description by Argani et al. Recognition of this entity can spare a child from potentially toxic adjuvant chemotherapy that might be used to treat malignant lesions which are part of the differential diagnosis, particularly clear cell sarcoma of kidney (CCSK).


**AUTORES / AUTHORS:** Khutti SD; Kumar RP; Sampath K

**INSTITUCIÓN / INSTITUTION:** Department of General Pathology, Christian Medical College and Hospital, Vellore, Tamilnadu, India.

**RESUMEN / SUMMARY:** It is still in high demand to develop extremely sensitive and accurate clinical tools for biomarkers of interest for early diagnosis and monitoring of diseases. In this report, we present a highly sensitive and compatible gold nanoparticle (AuNP)-based fluorescence-activatable probe for sensing ultralow levels of prostate-specific antigen (PSA) in patient serum samples. The limit of detection of the newly developed probe for PSA was pushed down to 0.032 pg/mL, which is more than 2 orders of magnitude lower than that of the conventional fluorescence probe. The ultrahigh sensitivity of this probe was attributed to the high loading efficiency of the dyes on AuNP surfaces and high fluorescence quenching-unquenching abilities of the dye-AuNP pairs. The efficiency and robustness of this probe were investigated in patient serum samples, demonstrating the great potential of this probe in real-world applications.

**REVISTA / JOURNAL:** ACS Nano. 2013 May 22.

**AUTORES / AUTHORS:** Liu D; Huang X; Wang Z; Jin A; Sun X; Zhu L; Wang F; Ma Y; Niu G; Hight Walker AR; Chen X

**INSTITUCIÓN / INSTITUTION:** Laboratory of Molecular Imaging and Nanomedicine, National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health, Bethesda, Maryland 20892, United States.
RESUMEN / SUMMARY: - Overexpression of tumour-associated carbohydrate antigen sialyl-Tn in advanced bladder tumours.

AUTORES / AUTHORS: - Ferreira JA; Videira PA; Lima L; Pereira S; Silva M; Carrascal M; Severino PF; Fernandes E; Almeida A; Costa C; Vitorino R; Amaro T; Oliveira MJ; Reis CA; Dall’olio F; Amado F; Santos LL

INSTITUCIÓN / INSTITUTION: - QOPNA, Mass Spectrometry Center, Department of Chemistry, University of Aveiro, Aveiro, Portugal; Experimental Pathology and Therapeutics Group, Portuguese Institute of Oncology, Porto, Portugal. Electronic address: alexandrecastroferreira@gmail.com.

RESUMEN / SUMMARY: - Little is known on the expression of the tumour-associated carbohydrate antigen sialyl-Tn (STn), in bladder cancer. We report here that 75% of the high-grade bladder tumours, presenting elevated proliferation rates and high risk of recurrence/progression expressed STn. However, it was mainly found in non-proliferative areas of the tumour, namely in cells invading the basal and muscle layers. STn was also found in tumour-adjacent mucosa, which suggests its dependence on a field effect of the tumour. Furthermore, it was not expressed by the normal urothelium, demonstrating the cancer-specific nature of this antigen. STn expression correlated with that of sialyltransferase ST6GalNAc.I, its major biosynthetic enzyme. The stable expression of ST6GalNAc.I in the bladder cancer cell line MCR induced STn expression and a concomitant increase of cell motility and invasive capability. Altogether, these results indicate for the first time a link between STn expression and malignancy in bladder cancer. Hence, therapies targeting STn may constitute new treatment approaches for these tumours.

[1467]

RESUMEN / SUMMARY: - Radiotherapy in the management of prostate cancer after radical prostatectomy.

AUTORES / AUTHORS: - Bartkowiak D; Bottke D; Wiegel T

INSTITUCIÓN / INSTITUTION: - Radiation Oncology Department, University Hospital Ulm, Ulm, Germany.

RESUMEN / SUMMARY: - The choice of treatment options for prostate cancer patients who have undergone radical prostatectomy depends on their risk profile, which is determined by the tumor node metastasis (TNM) status,
histopathologic findings, and the pre- and post-radical prostatectomy PSA characteristics. The results of large clinical studies with a 10-year follow-up or more are the backbone of predictive models for risk estimates that incorporate these criteria and also for guideline recommendations. For low-to-intermediate-risk prostate cancer patients and older patients, observation with - in case of biochemical recurrence - early salvage radiotherapy can be advised after R0 resection, thus, avoiding overtreatment. After R1 resection, adjuvant radiotherapy should be considered. Patients with two or more positive lymph nodes and/or with distant metastasis may benefit from adjuvant hormone deprivation therapy. Beyond this rough outline, detailed analysis of subgroups is still required (and ongoing) to enable individually optimized treatment.

[1468]

**TÍTULO / TITLE:**  - Sphingolipids’ role in radiotherapy for prostate cancer.

**RESUMEN / SUMMARY:**  - Enlace al Resumen / Link to its Summary


-●●Enlace al texto completo (gratuito o de pago) 1007/978-3-7091-1511-4_6.

**AUTORES / AUTHORS:**  - Hajj C; Haimovitz-Friedman A

**INSTITUCIÓN / INSTITUTION:**  - Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, 10065, USA, hajjc@mskcc.org.

**RESUMEN / SUMMARY:**  - There are several well-established mechanisms involved in radiation-induced cell death in mammalian cell systems. The p53-mediated apoptotic pathway is the most widely recognized mechanism (Lowe et al. Nature 362:847-849, 1993), although apoptosis has long been considered a less relevant mechanism of radiation-induced cell death (Steel, Acta Oncol 40:968-975, 2001; Brown and Wouters, Cancer Res 59:1391-1399, 1999; Olive and Durand, Int J Radiat Biol 71:695-707, 1997). We and others have recently focused instead on the emerging links between radiation, apoptosis, and ceramide and showed that ceramide is a sphingolipid-derived second messenger capable of initiating apoptotic cascades in response to various stress stimuli, including radiation. Ceramide, the backbone of all sphingolipids, is synthesized by a family of ceramide synthases (CerS), each using acyl-CoAs of defined chain length for N-acylation of the sphingoid long-chain base. Six mammalian CerS homologs have been cloned that demonstrated high selectivity towards acyl-CoAs (Lahiri et al. FEBS Lett 581:5289-5294, 2007), and more recently, it was shown that their activity can be modulated by dimer formation (Mesicek et al. Cell Signal 22:1300-1307, 2010; Laviad et al. J Biol Chem 283:5677-5684, 2008). This de novo ceramide synthesis has been observed in irradiated cells through a pathway normally suppressed by ataxia telangiectasia-mutated (ATM) protein, a key component of the cellular response.
to DNA double-strand breaks (Liao et al. J Biol Chem 274:17908-17917, 1999). ATM is not the sole factor known to affect apoptotic potential by modulating CerS activity. Recent work has also implicated protein kinase Calpha (PKCalpha) as a potential CerS activator (Truman et al. Cancer Biol Ther 8:54-63, 2009). In this review, we summarize involvement of CerS in sphingolipid-mediated apoptosis in irradiated human prostate cancer cells and discuss future directions in this field.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Valdagni R; Rancati T
INSTITUCIÓN / INSTITUTION: - 1] Department of Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1, Milan 20133, Italy [2] Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1, Milan 20133, Italy.
RESUMEN / SUMMARY: - Rectal bleeding and faecal incontinence are serious injuries that men with prostate cancer who receive radiotherapy can experience. Although technical advances-including the use of intensity-modulated radiotherapy coupled with image-guided radiotherapy-have enabled the delivery of dose distributions that conform to the shape of the tumour target with steep dose gradients that reduce the dose given to surrounding tissues, radiotherapy-associated toxicity can not be avoided completely. Many large-scale prospective studies have analysed the correlations of patient-related and treatment-related parameters with acute and late toxicity to optimize patient selection and treatment planning. The careful application of dose-volume constraints and the tuning of these constraints to the individual patient’s characteristics are now considered the most effective ways of reducing rectal morbidity. Additionally, the use of endorectal balloons (to reduce the margins between the clinical target volume and planning target volume) and the insertion of tissue spacers into the region between the prostate and anterior rectal wall have been investigated as means to further reduce late rectal injury. Finally, some drugs and other compounds are also being considered to help protect healthy tissue. Overall, a number of approaches exist that must be fully explored in large prospective trials to address the important issue of rectal toxicity in prostate cancer radiotherapy.

[1470] TÍTULO / TITLE: - Vesicocutaneous fistula following adjuvant radiotherapy for prostate cancer.
RESUMEN / SUMMARY: - Vesicocutaneous fistulas (VCF) are a rare complication of radical radiotherapy to the pelvis. Timely diagnosis and management are often difficult and complex. We report the unusual case of a 64-year-old gentleman who presented to the emergency department with worsening sepsis and profuse discharge from a cutaneous opening in the left groin. This presentation was 6 weeks following the completion of external beam radiotherapy for apical margin-positive prostate cancer (pT3a). A diagnosis of a VCF was confirmed after CT scanning of the abdomen and pelvis with contrast. Urinary diversion was achieved by a temporary urethral catheter insertion. Full resolution of this gentleman’s symptoms was accomplished. In this article, we present a non-invasive approach to the management of VCF. This case raises intricate management issues in the atypical development of an early urinary tract fistula postradiotherapy.

[1471]


RESUMEN / SUMMARY: - PURPOSE: Stereotactic body radiotherapy (SBRT) is being used with increasing frequency as definitive treatment of early stage prostate cancer. Much of the justification for its adoption was derived from earlier clinical results using high-dose-rate (HDR) brachytherapy. We determine whether HDR’s dosimetry can be achieved by virtual SBRT. METHODS AND
MATERIALS: Patients with intermediate-risk prostate cancer on a prospective trial evaluating the efficacy of HDR monotherapy treated to dose of 9.5Gy×4 fractions were used for this study. A total of 5 patients were used in this analysis. Virtual SBRT plans were developed to reproduce the planning target volume (PTV) HDR dose distributions. Both normal tissue- and PTV-prioritized plans were generated. RESULTS: From the normal tissue-prioritized plan, HDR and virtual SBRT achieved similar PTV V100 (93.8% vs. 93.1%, p=0.20) and V150 (40.3% vs. 42.9%, p=0.69) coverage. However, the PTV V200 was not attainable with SBRT (15.2% vs. 0.0%, p<0.001). The rectal Dmax was significantly lower with HDR (94.2% vs. 99.4%, p=0.05). The rectal D2 cc was also lower (60.8% vs. 71.1%, p=0.07). Difference in D1 cc urethral dose was not significantly different (87.7% vs. 75.2%, p=0.33). Comparing the PTV-prioritized plans, the rectal Dmax (94.2% vs. 111.1%, p=0.05) and mean dose (27.1% vs. 33.3%, p=0.03) were significantly higher using SBRT, and the rectal D2 cc was higher using SBRT (60.8% vs. 81.8%, p=0.07). CONCLUSIONS: HDR achieves significantly higher intraprostatic doses while achieving a lower maximum rectal dose compared with our virtual SBRT treatment planning. Future studies should compare clinical outcomes and toxicity between these modalities.

[1472]
TI TULO / TITLE: - Relationship of postoperative recatheterization and intraoperative bladder distention volume in holmium laser enucleation of the prostate for benign prostatic hyperplasia.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kim HJ; Lee HY; Song SH; Paick JS
INSTITUCIÓN / INSTITUTION: - Department of Urology, Seoul National University Hospital, Seoul, Korea.
RESUMEN / SUMMARY: - PURPOSE: The purpose of this study was to identify the risk factors for recatheterization after holmium laser enucleation of the prostate (HoLEP). MATERIALS AND METHODS: A total of 166 consecutive patients treated with HoLEP by a single surgeon from January 2010 to June 2011 were enrolled in this study. We collected data on preoperative and intraoperative parameters, including intraoperative bladder distention volume. The patients were divided into two groups. Group 1 included patients who voided successfully after removal of the catheter, and group 2 included patients who required recatheterization. Analysis and comparison of the perioperative parameters of both groups was performed for identification of risk factors for recatheterization. RESULTS: Recatheterization was required in 9 of 166 (5.4%) patients. No significant differences in age or preoperative parameters, including
prostate-specific antigen, prostate volume, International Prostate Symptom Score, peak flow rate, postvoid residual urine, maximal bladder capacity, and Abrahams Griffiths number, were observed between the two groups. Of the intraoperative parameters, intraoperative bladder distention volume was significantly smaller in group 1 than in group 2 (700.65 mL vs. 897.78 mL, p<0.001). In the multivariate logistic regression analysis, after adjustment for other variables, intraoperative bladder distention volume was found to be a statistically significant risk factor for postoperative recatheterization (hazard ratio, 1.006; confidence interval, 1.002 to 1.010; p=0.002). CONCLUSIONS: Nine of 166 (5.4%) patients failed to void after HoLEP and required catheterization. Intraoperative bladder distention volume was found to be a statistically significant risk factor for recatheterization in this patient group.

[1473]
**TÍTULO / TITLE:** - Extensive peritoneal carcinomatosis secondary to renal cell carcinoma with sarcomatoid and rhabdoid differentiation.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**REVISTA / JOURNAL:** - British Medical J (BMJ). Acceso gratuito al texto completo.

- Enlace a la Editora de la Revista [http://bmj.com/search.dtl](http://bmj.com/search.dtl)
- Enlace al texto completo (gratuito o de pago) [1136/bcr-2013-008725](1136/bcr-2013-008725)

**AUTORES / AUTHORS:** - Esnakula AK; Naab TJ; Green W; Shokrani B
**INSTITUCIÓN / INSTITUTION:** - Department of Pathology, Howard University Hospital, Washington, District of Columbia, USA. aesenakula@howard.edu
**RESUMEN / SUMMARY:** - Renal cell carcinoma (RCC), the most common malignancy of kidney, originates from renal tubular epithelium. It is subclassified based on histological and molecular features. Rarely, RCC can show focal to extensive sarcomatoid or rhabdoid differentiation. RCC with extensive sarcomatoid differentiation and no identifiable epithelial component is designated as unclassified RCC with sarcomatoid differentiation. Presence of sarcomatoid or rhabdoid differentiation is associated with poor prognosis. We describe autopsy findings in a case of RCC with extensive sarcomatoid and focal rhabdoid differentiation presenting with malignant ascites secondary to peritoneal carcinomatosis and multiorgan metastasis.

[1474]
**TÍTULO / TITLE:** - Comparison of radiographic and pathologic sizes of renal tumors.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
**AUTORES / AUTHORS:** - Chen W; Wang L; Yang Q; Liu B; Sun Y  
**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Changhai Hospital, Second Military Medical University, Shanghai, China.  
**RESUMEN / SUMMARY:** - Purpose: The determination of the size of a renal tumor is important for staging, prognosis and selection of the appropriate surgical treatment. We investigated the difference of radiographic and pathologic size of renal tumors in a contemporary cohort of patients who underwent nephron sparing surgery and evaluated its clinical implications. Materials and Methods: The records of 169 patients who received nephron sparing surgery for renal lesions suspicious for malignancy between January 2006 and December 2010 were reviewed retrospectively. Radiographic tumor size, defined as the largest diameter of tumor measured by CT images, and pathologic size, the largest diameter of tumor measured in the surgical specimen, were compared and analyzed. Results: Among all subjects, mean radiographic and pathologic tumor size were 3.25 +/- 1.78 cm and 3.03 +/- 1.91 cm, respectively (P < 0.001), with a discrepancy of just 0.22 cm. When the patients were categorized according to radiographic tumor size in the 1 cm range, the mean radiographic tumor size was significantly greater than pathologic tumor size in the following groups: 2 to 3 cm (P < 0.001), 3 to 4 cm (P < 0.001), and 4 to 5 cm (P = 0.028). When radiographic and pathologic tumor sizes were compared according to the pathologic tumor subtype, a significant difference was observed only among those with clear cell renal carcinoma (P < 0.001). Conclusions: Renal tumor size was overestimated by radiography as compared with pathology. The difference was just 0.22 cm with little clinical significance, suggesting that CT provides an accurate method to estimate renal tumor size preoperatively.

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**TITULO / TITLE:** - Towards ultrasound probe positioning optimization during prostate needle biopsy using pressure feedback.  
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary  
   ●●Enlace al texto completo (gratuito o de pago) 1007/s11548-013-0898-3  
**AUTORES / AUTHORS:** - Mousavi SR; Raahemifar K; Pautler S; Samani A  
**INSTITUCIÓN / INSTITUTION:** - Department of Electrical and Computer Engineering, Western University, London, ON, Canada, smousav8@uwo.ca.  
**RESUMEN / SUMMARY:** - PURPOSE: Accurate Transrectal Ultrasound (TRUS)-guided prostate needle biopsy requires registering preoperative 3D TRUS or MR image, in which tumors and other suspicious areas are visible, to intraoperative 2D TRUS images. Such image registration is time-consuming while its real-time implementation is yet to be developed. To bypass this registration step, robotic needle biopsy systems can be used to place the US probe at the same position relative to the prostate during the 3D and 2D image.
acquisition to ensure similar prostate deformation. To have such similar deformation, only visual feedback is not sufficient as such feedback can be used to only guarantee that the whole prostate is within the field of view irrespective of the probe’s orientation. As such, contact pressure feedback can be utilized to ensure consistent minimum contact between the probe and prostate. METHOD: A robotic system is proposed where a TRUS probe with pressure sensor array is used. The contact pressure can be measured during imaging and used to provide feedback in conjunction with an optimization algorithm for consistent probe positioning. The robotic system is driven by the feedback to position the probe such that pressure pattern of the sensors during 2D image acquisition is similar to the pressure pattern during 3D image acquisition. The proposed method takes into account the patient’s body movement expected during image acquisition. In this study, an in silico phantom is used where the simulated contact pressure distribution required in the optimization algorithm is obtained using a prostate finite element model. RESULT: Starting from an arbitrary position where the probe contacts the phantom, this position was varied systematically until a position corresponding to maximum pressure pattern similarity between contact pressure patterns corresponding to the 2D and 3D imaging was achieved successfully. CONCLUSION: Results obtained from the in silico phantom study indicate that the proposed technique is capable of ensuring having only minimal relative prostate deformation between preoperative image acquisition and intraoperative imaging used for guiding needle biopsy, paving the way for faster and more accurate registration.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Griwan MS; Kumar A; Sen J; Singh SK
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Pandit B.D.Sharma University of Health Sciences, Rohtak, India.
RESUMEN / SUMMARY: - BACKGROUND: The aim of the present study was to compare two analgesic techniques for transrectal ultrasound (TRUS)-guided biopsy: diclofenac patch versus periprostatic nerve block with 1% lidocaine. OBJECTIVES: To study the efficacy of and compare diclofenac patch and periprostatic nerve block as analgesia in TRUS-guided prostate needle biopsy. PATIENTS AND METHODS: In total, 60 patients were prospectively randomized into three groups: those in whom a diclofenac patch was used (n = 20), those in whom periprostatic nerve block was used (n = 20), and a control
group (n = 20). Prostate biopsy was performed after administration of analgesia according to group. RESULTS: The three groups were similar in terms of age, prostate volume, and PSA (prostate-specific antigen) levels. Pain scores were significantly lower in the nerve block group (P = 0.000) at the time of biopsy until 2 h postprocedure, but not at 4 h postprocedure (P = 0.068). No significant difference in pain score was observed in the diclofenac patch group at the time of biopsy (P = 0.106) as compared to the control group, but the diclofenac patch provided adequate pain relief 1 h (P = 0.000), 2 h (0.000), and 4 h (0.002) postprocedure. No significant difference was observed in pain score between the nerve block (P = 0.520) and control groups (0.057) at probe insertion. The pain score at 4 h was significantly lower in the patch group compared to the nerve block and control groups. CONCLUSIONS: Periprostatic nerve block provides superior analgesia for TRUS-guided biopsy. Diclofenac patch is useful as an adjunct.

[1477]

TÍTULO / TITLE: - Alterations of Histone H1 Phosphorylation During Bladder Carcinogenesis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1021/pr400143x
AUTORES / AUTHORS: - Telu KH; Abbaoui B; Thomas-Ahner JM; Zynger DL; Clinton SK; Freitas MA; Mortazavi A
RESUMEN / SUMMARY: - There is a crucial need for development of prognostic and predictive biomarkers in human bladder carcinogenesis in order to personalize preventive and therapeutic strategies and improve outcomes. Epigenetic alterations, such as histone modifications, are implicated in the genetic dysregulation that is fundamental to carcinogenesis. Here we focus on profiling the histone modifications during the progression of bladder cancer. Histones were extracted from normal human bladder epithelial cells, an immortalized human bladder epithelial cell line (hTERT), and four human bladder cancer cell lines (RT4, J82, T24, and UMUC3) ranging from superficial low-grade to invasive high-grade cancers. Liquid Chromatography-Mass Spectrometry (LC-MS) profiling revealed a statistically significant increase in phosphorylation of H1 linker histones from normal human bladder epithelial cells to low-grade superficial to high-grade invasive bladder cancer cells. This finding was further validated by immunohistochemical staining of the normal epithelium and transitional cell cancer from human bladders. Cell cycle analysis of histone H1 phosphorylation by western blotting showed an increase of phosphorylation from G0/G1 phase to M phase, again supporting this as a proliferative marker. Changes in histone H1 phosphorylation status may further clarify epigenetic changes during bladder carcinogenesis and provide diagnostic and prognostic biomarkers or targets for future therapeutic interventions.
[1478]
**TÍTULO / TITLE:** Renal cell carcinoma seeding of a percutaneous biopsy tract.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 5489/cuaj.499
**AUTORES / AUTHORS:** Mullins JK; Rodriguez R
**INSTITUCIÓN / INSTITUTION:** James Buchanan Brady Urological Institute, Johns Hopkins Medical Institutions, Baltimore, MD.
**RESUMEN / SUMMARY:** We report the case of a 68-year-old male with extension of papillary renal cell carcinoma (Fuhrman grade III) along a percutaneous biopsy tract detected at the time of partial nephrectomy. Biopsy was performed to obtain tissue diagnosis of a complex renal cyst as the patient was unable to receive intravenous contrast for imaging due to a severe allergy. Although biopsy of indeterminate renal lesions can provide valuable diagnostic information, there are inherent risks associated with this procedure. The rare occurrence of tumour seeding should be considered when recommending percutaneous biopsy to a patient with a renal mass.

[1479]
**TÍTULO / TITLE:** An in vitro assessment of panel of engineered nanomaterials using a human renal cell line: cytotoxicity, pro-inflammatory response, oxidative stress and genotoxicity.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1186/1471-2369-14-96
**AUTORES / AUTHORS:** Kermanizadeh A; Vranic S; Boland S; Moreau K; Baeza-Squiban A; Gaiser BK; Andrzejczuk LA; Stone V
**INSTITUCIÓN / INSTITUTION:** Heriot-Watt University, School of Life Sciences, John Muir building, Edinburgh, EH14 4AS, UK. A.Kermanizadeh@hw.ac.uk.
**RESUMEN / SUMMARY:** BACKGROUND: It has been shown that nanomaterials (NMs) are able to translocate to secondary tissues one of the important being the kidneys. Oxidative stress has been implicated as a possible mechanism for NM toxicity, hence effects on the human renal proximal tubule epithelial cells (HK-2) treated with a panel of engineered nanomaterials (NMs) consisting of two zinc oxide particles (ZnO-coated NM 110 and uncoated NM 111), two multi walled carbon nanotubes (MWCNT) (NM 400 and NM 402), one silver (NM 300) and five TiO2 NMs (NM 101, NRCWE 001, 002, 003 and 004) were evaluated. METHODS: In order to assess the toxicological impact of the engineered NMs on HK-2 cells - WST-1 cytotoxicity assay, FACSArray, HE oxidation and the comet assays were utilised. For statistical analysis, the
experimental values were compared to their corresponding controls using an ANOVA with Tukey’s multiple comparison. RESULTS: We found the two ZnO NMs (24 hr LC50 - 2.5 mg/cm²) and silver NM (24 hr LC50 - 10 mg/cm²) were highly cytotoxic to the cells. The LC50 was not attained in the presence of any of the other engineered nanomaterials (up to 80 mg/cm²). All nanomaterials significantly increased IL8 and IL6 production. Meanwhile no significant change in TNF-alpha or MCP-1 was detectable. The most notable increase in ROS was noted following treatment with the Ag and the two ZnO NMs. Finally, genotoxicity was measured at sub-lethal concentrations. We found a small but significant increase in DNA damage following exposure to seven of the ten NMs investigated (NM 111, NRCWE 001 and NRCWE 003 being the exception) with this increase being most visible following exposure to Ag and the positively charged TiO2. CONCLUSIONS: While the NMs could be categorised as low and highly cytotoxic, sub-lethal effects such as cytokine production and genotoxicity were observed with some of the low toxicity materials.

[1480]

TÍTULO / TITLE: - Targeting both IGF-1R and mTOR synergistically inhibits growth of renal cell carcinoma in vitro.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Cardillo TM; Trisal P; Arrojo R; Goldenberg DM; Chang CH

INSTITUCIÓN / INSTITUTION: - Immunomedics, Inc, 300 American Rd, Morris Plains, NJ 07950, USA. tcardillo@immunomedics.com

RESUMEN / SUMMARY: - BACKGROUND: Advanced or metastatic renal cell carcinoma (RCC) has a poor prognosis, because it is relatively resistant to conventional chemotherapy or radiotherapy. Treatments with human interferon-alpha2b alone or in combination with mammalian target of rapamycin (mTOR) inhibitors have led to only a modest improvement in clinical outcome. One observation made with mTOR inhibitors is that carcinomas can overcome these inhibitory effects by activating the insulin-like growth factor-I (IGF-I) signaling pathway. Clinically, there is an association of IGF-I receptor (IGF-IR) expression in RCC and poor long-term patient survival. We have developed a humanized anti-IGF-IR monoclonal antibody, hR1, which binds to RCC, resulting in effective down-regulation of IGF-IR and moderate inhibition of cell proliferation in vitro. In this work, we evaluate the anti-tumor activity of two novel IGF-1R-targeting agents against renal cell carcinoma given alone or in combination with an mTOR inhibitor. METHODS: hR1 was linked by the DOCK-AND-LOCK (DNL) method to four Fabs of hR1, generating Hex-hR1, or to four molecules of
interferon-alpha2b, generating 1R-2b. Eight human RCC cell lines were screened for IGF-1R expression and sensitivity to treatment with hR1 in vitro. Synergy with an mTOR inhibitor, temsirolimus, was tested in a cell line (ACHN) with low sensitivity to hR1. RESULTS: Hex-hR1 induced the down-regulation of IGF-IR at 10-fold lower concentrations compared to the parental hR1. Sensitivity to growth inhibition mediated by hR1 and Hex-hR1 treatments correlated with IGF-1R expression (higher expression was more sensitive). The potency of 1R-2b to inhibit the in vitro growth of RCC was also demonstrated in two human cell lines, ACHN and 786-O, with EC50-values of 63 and 48 pM, respectively. When combined with temsirolimus, a synergistic growth-inhibition with hR1, Hex-hR1, and 1R-2b was observed in ACHN cells at concentrations as low as 10 nM for hR1, 1 nM for Hex-hR1, and 2.6 nM for 1R-2b.

CONCLUSIONS: Both Hex-hR1 and 1R-2b proved to be more potent than parental hR1 in inhibiting growth of RCC in vitro. Synergy was achieved when each of the three hR1-based agents was combined with temsirolimus, suggesting a new approach for treating RCC.

[1481]
TÍTULO / TITLE: - Atypical small acinar proliferation: utility of additional sections and immunohistochemical analysis of prostatic needle biopsies.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Arista-Nasr J; Martinez-Mijangos O; Martinez-Benitez B; Bornstein-Quevedo L; Lino-Silva S; Urbina-Ramirez S
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Instituto Nacional de Ciencias Medica y la Nutricion, S. Z. (INCMNSZ), Tlalpan, Mexico D.F, Mexico.
RESUMEN / SUMMARY: - BACKGROUND: In surgical pathology, atypical small acinar proliferation is commonly detected in prostate biopsies. Most studies on atypical small acinar proliferation have examined morphological characteristics and the utility of immunohistochemical studies. However, these resources are not available to many pathology departments. We have found that examining additional sections is a simple and inexpensive method that allows better evaluation of focal prostatic glandular atypia. OBJECTIVES: The present report compares the diagnostic utility of immunohistochemical techniques versus examining additional sections in prostate biopsies with focal glandular atypia. PATIENTS AND METHODS: Thirty recently studied prostate biopsies with focal glandular atypia were selected. In each case, 3 additional levels were examined. An immunohistochemical study was performed on one level using an antibody against high-molecular-weight keratin (34BetaE12). Two additional sections were stained with hematoxylin and eosin. RESULTS: The diagnosis of focal carcinoma was established with only additional sections in 4 cases.
In 2 of these biopsies, additional areas of carcinoma were found that were not identified in the original sections. In 4 other cases, immunohistochemical analysis was the only useful method for diagnosing cancer. In 9 cases (30%), both methods were useful for classifying focal glandular atypia as carcinoma. In the remaining 13 cases, neither immunohistochemical analysis nor additional sections were useful in changing the diagnosis of focal glandular atypia. CONCLUSIONS: Focal glandular atypia in prostatic needle biopsies should be routinely examined with additional sections, particularly when immunohistochemical analysis is not possible. Some biopsies with atypical glandular proliferation may show focal carcinoma in additional sections, even if the immunohistochemical analysis did not provide a diagnosis of malignancy. Additional sections can also reveal areas of carcinoma that were not apparent in the original sections.

CONCLUSION S: Focal glandular atypia in prostatic needle biopsies should be routinely examined with additional sections, particularly when immunohistochemical analysis is not possible. Some biopsies with atypical glandular proliferation may show focal carcinoma in additional sections, even if the immunohistochemical analysis did not provide a diagnosis of malignancy. Additional sections can also reveal areas of carcinoma that were not apparent in the original sections.
from cells co-injected with Matrigel. In 40% of SISgel xenografts, growth resumed in the malignant phenotype after a period of suppression or dormancy for at least 30 days and was more likely with implantation of 3 million or more cells. Ordinary Type I collagen did not suppress malignant growth, and tumors developed about as well with collagen as with Matrigel. A clear signal in gene expression over different cell lines was not seen by transcriptome microarray analysis, but in contrast, Reverse Phase Protein Analysis of 250 proteins across 4 cell lines identified Integrin Linked Kinase (ILK) signaling that was functionally confirmed by an ILK inhibitor. We suggest that cancer cells suppressed on SISgel could serve as a model for dormancy and re-awakening to allow for the identification of therapeutic targets for treating micrometastases.

[1483]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

●●Enlace al texto completo (gratuito o de pago)
1371/journal.pone.0059536
AUTORES / AUTHORS: - Jager W; Moskalev I; Janssen C; Hayashi T; Awrey S; Gust KM; So AI; Zhang K; Fazli L; Li E; Thuroff JW; Lange D; Black PC
INSTITUCIÓN / INSTITUTION: - The Vancouver Prostate Centre and Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada.
RESUMEN / SUMMARY: - Orthotopic bladder cancer xenografts are essential for testing novel therapies and molecular manipulations of cell lines in vivo. Current xenografts rely on tumor cell inoculation by intravesical instillation or direct injection into the bladder wall. Instillation is limited by the lack of cell lines that are tumorigenic when delivered in this manner. The invasive model inflicts morbidity on the mice by the need for laparotomy and mobilization of the bladder. Furthermore this procedure is complex and time-consuming. Three bladder cancer cell lines (UM-UC1, UM-UC3, UM-UC13) were inoculated into 50 athymic nude mice by percutaneous injection under ultrasound guidance. PBS was first injected between the muscle wall and the mucosa to separate these layers, and tumor cells were subsequently injected into this space. Bioluminescence and ultrasound were used to monitor tumor growth. Contrast-enhanced ultrasound was used to study changes in tumor perfusion after systemic gemcitabine/cisplatin treatment. To demonstrate proof of principle that therapeutic agents can be injected into established xenografts under ultrasound guidance, oncolytic virus (VSV) was injected into UM-UC3 tumors. Xenograft tissue was harvested for immunohistochemistry after 23-37 days. Percutaneous injection of tumor cells into the bladder wall was performed efficiently (mean time: 5.7 min) and without complications in all 50 animals. Ultrasound and
bioluminescence confirmed presence of tumor in the anterior bladder wall in all animals 3 days later. The average tumor volumes increased steadily over the study period. UM-UC13 tumors showed a marked decrease in volume and perfusion after chemotherapy. Immunohistochemical staining for VSV-G demonstrated virus uptake in all UM-UC3 tumors after intratumoral injection. We have developed a novel method for creating orthotopic bladder cancer xenograft in a minimally invasive fashion. In our hands this has replaced the traditional model requiring laparotomy, because this model is more time efficient, more precise and associated with less morbidity for the mice.

[1484]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.73

[1485]
TITULO / TITLE: - The role of aberrant promoter hypermethylation of DACT1 in bladder urothelial carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 7555/JBR.26.20110099
AUTORES / AUTHORS: - Cheng H; Deng Z; Wang Z; Zhang W; Su J
INSTITUCIÓN / INSTITUTION: - Department of Urology, the First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu 210029, China.
RESUMEN / SUMMARY: - The purpose of this study was to determine the relationship between hypermethylation of DACT1 gene promoter and lower mRNA expression in bladder urothelial carcinoma tissue. The methylation status of 29 urothelial carcinoma samples and 29 normal tissue samples were examined by methylation-specific polymerase chain reaction (MSP). The DACT1 mRNA transcript levels and DACT1 protein levels in all samples were then evaluated to define the relationship between the methylation status of the DACT1 promoter and its expression at the transcriptional and translational levels. Decreased expression of DACT1 was detected in 89.66% of urothelial carcinomas (26/29; P < 0.005). Promoter hypermethylation was found in 58.62% (17/29) urothelial carcinomas and 25% (7/29) normal tissues, respectively (P < 0.05). DACT1 expression was lower in tissues where the DACT1 gene promoter was hypermethylated than in unmethylated tissues (0.25+-0.17 vs 0.69+-0.30, P < 0.05). DACT1 gene hypermethylation was closely related to tumor size, grade and stage (P < 0.05). Our results indicate
that silencing and downregulation of DACT1 mRNA may be implicated in carcinogenesis and the progression of bladder urothelial carcinoma, and may be a potential prognostic factor.

[1486]
TÍTULO / TITLE: - Small renal masses: The effect of illness uncertainty during active surveillance.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Crispen PL
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[1487]
TÍTULO / TITLE: - Small renal masses: The promise of thulium laser enucleation partial nephrectomy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Guzzo TJ
INSTITUCIÓN / INSTITUTION: - The Hospital of the University of Pennsylvania, The Perelman Center for Advanced Medicine, West Pavilion, 3rd Floor, 3400 Civic Center Boulevard, Philadelphia, PA 19104, USA. thomas.guzzo@uphs.upenn.edu.

[1488]
TÍTULO / TITLE: - Spermine and citrate as metabolic biomarkers for assessing prostate cancer aggressiveness.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Giskeodegard GF; Bertilsson H; Selnaes KM; Wright AJ; Bathen TF; Viset T; Halgunset J; Angelsen A; Gribbestad IS; Tessem MB
INSTITUCIÓN / INSTITUTION: - MI Lab, Department of Circulation and Medical Imaging, Norwegian University of Science and Technology (NTNU), Trondheim, Norway ; St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway.
RESUMEN / SUMMARY: - Separating indolent from aggressive prostate cancer is an important clinical challenge for identifying patients eligible for active surveillance, thereby reducing the risk of overtreatment. The purpose of this study was to assess prostate cancer aggressiveness by metabolic profiling of prostatectomy tissue and to identify specific metabolites as biomarkers for aggressiveness. Prostate tissue samples (n = 158, 48 patients) with a high cancer content (mean: 61.8%) were obtained using a new harvesting method, and metabolic profiles of samples representing different Gleason scores (GS) were acquired by high resolution magic angle spinning magnetic resonance spectroscopy (HR-MAS). Multivariate analysis (PLS, PLS-DA) and absolute quantification (LCModel) were used to examine the ability to predict cancer aggressiveness by comparing low grade (GS = 6, n = 30) and high grade (GS>/=7, n = 81) cancer with normal adjacent tissue (n = 47). High grade cancer tissue was distinguished from low grade cancer tissue by decreased concentrations of spermine (p = 0.0044) and citrate (p = 7.73.10(-4)), and an increase in the clinically applied (total choline+creatine+polyamines)/citrate (CCP/C) ratio (p = 2.17.10(-4)). The metabolic profiles were significantly correlated to the GS obtained from each tissue sample (r = 0.71), and cancer tissue could be distinguished from normal tissue with sensitivity 86.9% and specificity 85.2%. Overall, our findings show that metabolic profiling can separate aggressive from indolent prostate cancer. This holds promise for the benefit of applying in vivo magnetic resonance spectroscopy (MRS) within clinical MR imaging investigations, and HR-MAS analysis of transrectal ultrasound-guided biopsies has a potential as an additional diagnostic tool.

[1489]

TÍTULO / TITLE: - A role for cytosolic fumarate hydratase in urea cycle metabolism and renal neoplasia.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Adam J; Yang M; Bauerschmidt C; Kitagawa M; O’Flaherty L; Maheswaran P; Ozkan G; Sahgal N; Baban D; Kato K; Saito K; Iino K; Igarashi K; Stratford M; Pugh C; Tennant DA; Ludwig C; Davies B; Ratcliffe PJ; El-Bahrawy M; Ashrafian H; Soga T; Pollard PJ

INSTITUCIÓN / INSTITUTION: - Cancer Biology and Metabolism Group, Nuffield Department of Medicine, Henry Wellcome Building for Molecular Physiology, University of Oxford, Oxford OX3 7BN, UK.

RESUMEN / SUMMARY: - The identification of mutated metabolic enzymes in hereditary cancer syndromes has established a direct link between metabolic dysregulation and cancer. Mutations in the Krebs cycle enzyme, fumarate
hydratase (FH), predispose affected individuals to leiomyomas, renal cysts, and cancers, though the respective pathogenic roles of mitochondrial and cytosolic FH isoforms remain undefined. On the basis of comprehensive metabolomic analyses, we demonstrate that FH1-deficient cells and tissues exhibit defects in the urea cycle/arginine metabolism. Remarkably, transgenic re-expression of cytosolic FH ameliorated both renal cyst development and urea cycle defects associated with renal-specific FH1 deletion in mice. Furthermore, acute arginine depletion significantly reduced the viability of FH1-deficient cells in comparison to controls. Our findings highlight the importance of extramitochondrial metabolic pathways in FH-associated oncogenesis and the urea cycle/arginine metabolism as a potential therapeutic target.

TÍTULO / TITLE: Metabolomic profiling of lung and prostate tumor tissues by capillary electrophoresis time-of-flight mass spectrometry.
RESUMEN / SUMMARY: Metabolic microenvironment of tumor cells is influenced by oncogenic signaling and tissue-specific metabolic demands, blood supply, and enzyme expression. To elucidate tumor-specific metabolism, we compared the metabolomics of normal and tumor tissues surgically resected pairwise from nine lung and seven prostate cancer patients, using capillary electrophoresis time-of-flight mass spectrometry (CE-TOFMS). Phosphorylation levels of enzymes involved in central carbon metabolism were also quantified. Metabolomic profiles of lung and prostate tissues comprised 114 and 86 metabolites, respectively, and the profiles not only well distinguished tumor from normal tissues, but also squamous cell carcinoma from the other tumor types in lung cancer and poorly differentiated tumors from moderately differentiated tumors in prostate cancer. Concentrations of most amino acids, especially branched-chain amino acids, were significantly higher in tumor tissues, independent of organ type, but of essential amino acids were particularly higher in poorly differentiated than moderately differentiated prostate cancers. Organ-dependent differences were prominent at the levels of glycolytic and tricarboxylic acid cycle intermediates and associated energy status. Significantly high lactate concentrations and elevated activating phosphorylation levels of
phosphofructokinase and pyruvate kinase in lung tumors confirmed hyperactive glycolysis. We highlighted the potential of CE-TOFMS-based metabolomics combined with phosphorylated enzyme analysis for understanding tissue-specific tumor microenvironments, which may lead to the development of more effective and specific anticancer therapeutics.

[1491]
TÍTULO / TITLE: - Impact of experience and technical changes on acute urinary and rectal morbidity in low-dose prostate brachytherapy using loose seeds real-time implantation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●●Enlace al texto completo (gratuito o de pago) 1016/j.brachy.2013.04.002
AUTORES / AUTHORS: - Le Fur E; Malhaire JP; Nowak E; Rousseau B; Erauso A; Pene-Baverez D; Papin G; Delage F; Perrouin-Verbe MA; Fournier G; Pradier O; Valeri A
INSTITUCIÓN / INSTITUTION: - Radiation Therapy Department, Centre Hospitalier Universitaire Morvan, Brest, France; Faculte de Medecine et des Sciences de la Sante, Universite de Bretagne Occidentale, Brest, France; Inserm U650, Laboratoire de Traitement de l'Information Medicale, Brest, France. Electronic address: emmanuelle.lefur@chu-brest.fr.
RESUMEN / SUMMARY: - PURPOSE: To assess the impact of experience and technical changes on morbidity during the first year after permanent prostate brachytherapy. METHODS AND MATERIALS: From July 2003 to May 2010, 150 patients with prostate cancer underwent low-dose iodine-125 prostate brachytherapy as a monotherapy by the same medical team (one urologist and one radiation oncologist). Patients were divided into three periods: P1 (n = 64), P2 (n = 45), and P3 (n = 41) according to technical changes: use of an automatic stepper from P2, use of a high-frequency ultrasound probe in P3. Urinary toxicity was analyzed according to the incidence of acute urinary retention (AUR), Delta International Prostate Symptom Score (Delta IPSS) defined as IPPS maximal - IPSS at baseline, and proportion of patients with Delta IPSS >/=5 and IPSS total >15. The Radiation Therapy Oncology Group classification was used to evaluate the rectal morbidity. RESULTS: The incidence of AUR (6% overall) decreased significantly with time: 12.5% (8/64) during P1, 2.2% (1/45) in P2, and 0% in P3 (p = 0.014). Mean Delta IPSS (11.6) remained stable during the three periods. Patients with Delta IPSS >/=5 and IPSS total >15 were 58.7%, 58.1%, and 56.1% for P1, P2, and P3 (p = 0.96), respectively. Grade 1 and 2 proctitis were observed in 15.3% and 9.3% of the patients without any significant difference between the three periods. CONCLUSION: The incidence of AUR decreased significantly with time. This
was probably because of the experience of the practitioner and the use of an automatic stepper that allowed reducing prostatic traumatism. Experience and technical changes did not seem to affect rectal morbidity.

[1492]
**Título / Title:** - The natural history of secondary muscle-invasive bladder cancer.

**Resumen / Summary:** - Enlace al Resumen / Link to its Summary


**Autores / Authors:** - Hidas G; Pode D; Shapiro A; Katz R; Appelbaum L; Pizov G; Zorn KC; Landau EH; Duvdevani M; Gofrit ON

**Institución / Institution:** - Department of Urology, Hadassah University Medical Center, Jerusalem, Israel. ogofrit@gmail.com.

**Resumen / Summary:** - BACKGROUND: The management of patients with high-grade non muscle invasive bladder cancer (NMIBC) brings diagnostic and therapeutic challenges. In the current study, we sought to study the natural history of progression to “secondary” muscle-invasive bladder cancer (MIBC)-cancer that developed during follow up of patients presenting with non-muscle invasive bladder cancer (NMIBC). METHODS: Between 1998 and 2008, 760 patients were treated for bladder cancer. Primary MIBC (>=T2) tumors (present upon presentation) were diagnosed in 114 patients. All patients with high-grade NMIBC were treated with intravesical BCG. Mean follow-up was 44 months. RESULTS: Forty patients (6.1%) developed secondary MIBC after a mean period of 21 months from initial diagnosis of bladder cancer. The 2- and 5-year disease-specific survival rates were better for patients with secondary MIBC (90% and 56% compared to 69% and 42% for patients with primary disease, p=0.03). The Kaplan-Meier curves of the two groups were parallel but displaced by approximately 2 years. CONCLUSION: In the current series, MIBC progression occurred among initially presenting patients with NMIBC in 6.1%. In most patients, the initial diagnosis of NMIBC is correct and muscle invasion occurs after a mean period of about 2 years. This supports a non-radical approach in patients with high-grade T1, Ta or Tis. Meticulous follow-up with liberal biopsy of any suspicious lesion may provide early diagnosis of invasive disease.

[1493]
**Título / Title:** - Microbiological characteristics of acute prostatitis after transrectal prostate biopsy.

**Resumen / Summary:** - Enlace al Resumen / Link to its Summary

PURPOSE: We aimed to identify microbiological characteristics in patients with acute prostatitis after transrectal prostate biopsy to provide guidance in the review of prevention and treatment protocols.

MATERIALS AND METHODS: A retrospective analysis of medical records was performed in 1,814 cases who underwent prostate biopsy at Seoul St. Mary’s Hospital and St. Vincent’s Hospital over a 5 year period from 2006 to 2011. Cases in which acute prostatitis occurred within 7 days after the biopsy were investigated. Before starting treatment with antibiotics, sample collections were done for culture of urine and blood. Culture and drug susceptibility was identified by use of a method established by the Clinical and Laboratory Standards Institute.

RESULTS: A total of 1,814 biopsy procedures were performed in 1,541 patients. For 1,246 patients, the procedure was the first biopsy, whereas for 295 patients it was a repeat biopsy. Twenty-one patients (1.36%) were identified as having acute bacterial prostatitis after the biopsy. Fifteen patients (1.2%) had acute prostatitis after the first biopsy, and 6 patients (2.03%) experienced acute prostatitis after a repeat biopsy. Even though the incidence of acute bacterial prostatitis was higher after repeat biopsy than that after the first biopsy, there was no statistically significant intergroup difference in terms of incidence (chi(2)=1.223, p=0.269). When the collected urine and blood samples were cultured, Escherichia coli was found in samples from 15 patients (71.4%), Klebsiella pneumoniae in 3 patients (14.3%), Enterobacter intermedius in 1 patient (4.8%), E. aerogenes in 1 patient (4.8%), and Pseudomonas aeruginosa in 1 patient (4.8%). A fluoroquinolone-resistant strain was confirmed in 5 cases (23.8%) in total. Three cases of E. coli and 1 case of Klebsiella had extended-spectrum beta-lactamase activity.

CONCLUSIONS: Empirical treatment of acute prostatitis should be done with consideration of geographical prevalence and drug resistance. This study will provide meaningful information for the management of acute prostatitis after transrectal prostate biopsy.
RESUMEN / SUMMARY: - OBJECTIVE: In sever oligospermia; one of the paths used for surgical sperm retrieval (SSR) is to extract sperm via a testicular biopsy. The aim of our study is to determine the reliable time interval between testicular biopsy and intracytoplasmic sperm injection (ICSI) procedure in order to obtain optimum sperm parameters (count, motility and normal morphology).

MATERIALS AND METHODS: This cohort study was carried out on 30 patients which were candidates for ICSI. After collection and keeping the samples obtained from the testicular biopsy in Ham’s F10 environment, the concentration, motility and morphology of the sperm in each sample was evaluated immediately as well as 2 and 4 hours after processing. The Data were then compared with each other. For the statistical analysis, Friedman, Wilcoxon and Cochrans tests were used. RESULTS: The mean of sperm concentration was 5.69 +/- 6.14 million and the motility was 10.83 +/- 12.63% at 2 hours following biopsy which was significantly higher than those obtained after 0 and 4 hours of the biopsy (p <0.05). CONCLUSION: The reliable preincubation time which resulted in the highest rate of spermatozoa parameters after testicular biopsy and before incubation was 2 hours.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Parr RL; Mills J; Harbottle A; Creed JM; Crewdson G; Reguly B; Guimont FS
INSTITUCIÓN / INSTITUTION: - Mitomics Inc., Suite 1000, 290 Munro St., Thunder Bay, Ontario P7A 7T1, Canada.
RESUMEN / SUMMARY: - Mitochondria and their associated genome are emerging as sophisticated indicators of prostate cancer biology. Alterations in the mitochondrial genome (mtgenome) have been implicated in cell proliferation, metastatic behavior, androgen independence, as a signal for apoptosis, and as a predictor of biochemical recurrence. Somatic mutation patterns in complete mtgenomes are associated with prostate specific antigen levels (PSA) in prostate cancer patients and a large-scale mtgenome deletion (3.4kb) is consistent with a prostate “cancerization” field effect. This review will focus on the biological characteristics of mitochondria and their direct clinical application to prostate cancer. Mitochondrial science is currently influencing clinical prostate cancer diagnostics and the rapid progress in this area indicates future, break-through contributions in the general field of oncology.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
To biopsy a small renal mass, or not?

Intravesical and transperitoneal laparoscopy in the management of tumor in the residual ureter.

The occurrence of tumor in the residual ureter after an incomplete nephroureterectomy required by a tumor of renal collecting system is an uncommon but a well described situation. The recommended treatment in this situation is the radical excision of the remaining ureter, being the open technique the most used approach. The aim of this video is to demonstrate a new approach using intravesical and transperitoneal laparoscopy to remove the residual ureter following the oncological concepts. A 67 year-old male patient underwent an incomplete open right radical nephroureterectomy for a transitional cell carcinoma of the renal collecting system. After 16 months, the cystoscopy diagnostic revealed a recurrence of it in the residual ureter. An intravesical approach followed by a transperitoneal laparoscopy has removed the remaining ureter. Operative time was 110 minutes, blood loss 100 mL, the patient was discharged on the first postoperative day and the Folley catheter was removed on the seventh one. Pathological examination revealed low grade transitional cell carcinoma and free surgical margins, no recurrence was observed after six months. To our knowledge, this is the first treatment.
description of a tumor in the residual ureter with these techniques. This approach can be a minimal invasive alternative in this unusual situation.

[1499]
**TÍTULO / TITLE:** - Small renal masses: Time to standardize follow-up of low-stage renal cancer.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)
  ●●Enlace al texto completo (gratuito o de pago) [1038/nrurol.2013.87](#)
**AUTORES / AUTHORS:** - Almatar A; Jewett MA
**INSTITUCIÓN / INSTITUTION:** - Department of Surgery, Division of Urology, Princess Margaret Cancer Centre, University Health Network, University of Toronto, 610 University Avenue, Suite 3-130, Toronto, ON M5G 2M9, Canada.

[1500]
**TÍTULO / TITLE:** - Efficacy of temsirolimus in metastatic chromophobe renal cell carcinoma.
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)
  ●●Enlace al texto completo (gratuito o de pago) [1186/1471-2490-13-26](#)
**AUTORES / AUTHORS:** - Venugopal B; Ansari J; Aitchison M; Tho LM; Campbell R; Jones RJ
**RESUMEN / SUMMARY:** - BACKGROUND: Renal cell carcinoma (RCC) is a histopathologically and molecularly heterogeneous disease with the chromophobe subtype (chRCC) accounting for approximately 5% of all cases. The median overall survival of advanced RCC has improved significantly since the advent of tyrosine kinase inhibitors and mammalian target of rapamycin (mTOR) inhibitors. However, high-quality evidence for the use of new generation tyrosine kinase inhibitors in patients with advanced chRCC is lacking. Few published case reports have highlighted the use of temsirolimus in chRCC. CASE PRESENTATION: Here, we report the case of a 36-year-old Caucasian woman with metastatic chRCC with predominantly skeletal metastases who was refractory to sunitinib who demonstrated a durable clinical response to temsirolimus lasting 20 months. We review the available evidence pertaining to the use of new generation molecularly targeted agents, in particular mTOR inhibitors in chRCC and discuss their emerging role in the management of this disease which would aid the oncologists faced with the challenge of treating this rare type of RCC. CONCLUSION: Conducting randomised clinical trials in this rarer sub-group of patients would be challenging and our case report and the evidence reviewed would guide the physicians to make informed decision regarding the management of these patients.
Sarcoidosis manifesting as a pseudotumorous renal mass.

A 53-year-old African American woman with a three-year history of pulmonary sarcoidosis had a follow-up computed tomographic scan to evaluate the status of her disease and response to treatment. On the scan, an abnormal, hypodense mass on the left renal superior pole, which was not present on previous scans, was incidentally discovered. The initial concern was of carcinoma, despite her lack of any urinary symptoms. She underwent further evaluation with magnetic resonance, and the enhancement pattern and the shape of the mass were more suggestive of lymphoma or infarction than a carcinoma. A review of literature revealed sparse case reports demonstrating sarcoidosis presenting as infiltrative granulomatous masses resembling tumors with nonspecific imaging qualities. This diagnosis was entertained and then proven by biopsy. Pseudotumorous renal sarcoid should be in the differential of renal masses, especially in patients with a history of sarcoidosis, as it alters clinical management.

Prostate brachytherapy can be used as a monotherapy for low- and intermediate-risk patients or in combination with external beam radiation therapy (EBRT) as a form of dose escalation for selected intermediate- and high-risk patients. Prostate brachytherapy with either permanent implants (low dose rate [LDR]) or temporary implants (high dose rate [HDR]) is emerging as the most effective radiation treatment for prostate cancer. Several large Canadian brachytherapy programs were established in the mid- to late-1990s. Prostate brachytherapy is offered in British Columbia, Alberta, and Manitoba.
Ontario, Quebec and New Brunswick. We anticipate the need for brachytherapy services in Canada will significantly increase in the near future. In this review, we summarize brachytherapy programs across Canada, contemporary eligibility criteria for the procedure, toxicity and prostate-specific antigen recurrence free survival (PRFS), as published from Canadian institutions for both LDR and HDR brachytherapy.

[1503]
TÍTULO / TITLE: - Prostate cancer: Prostatic swelling and shift upon HIFU.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.98
AUTORES / AUTHORS: - Clyne M

[1504]
TÍTULO / TITLE: - Potent anti-cancer effects of citrus peel flavonoids in human prostate xenograft tumors.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 1039/c3fo60037h
AUTORES / AUTHORS: - Lai CS; Li S; Miyauchi Y; Suzawa M; Ho CT; Pan MH
INSTITUCIÓN / INSTITUTION: - Department of Seafood Science, National Kaohsiung Marine University, No.142, Haijhuan Rd., Nanzih District, Kaohsiung 81143, Taiwan. mhpam@mail.nkmu.edu.tw.
RESUMEN / SUMMARY: - Prostate cancer is one of the most prevalent malignancies and is the second leading cause of cancer-related deaths in men. Fruit and vegetable consumption is a novel, non-toxic therapeutic approach that can be used to prevent and treat prostate cancer. Citrus peels and their extracts have been reported to have potent pharmacological activities and health benefits due to the abundance of flavonoids in citrus fruits, particularly in the peels. Our previous studies demonstrated that oral administration of Gold Lotion (GL), an extract of multiple varieties of citrus peels containing abundant flavonoids, including a large percentage of polymethoxyflavones (PMFs), effectively suppressed azoxymethane (AOM)-induced colonic tumorigenesis. However, the efficacy of GL against prostate cancer has not yet been investigated. Here, we explored the anti-tumor effects of GL using a human prostate tumor xenograft mouse model. Our data demonstrated that treatment with GL by both intraperitoneal (i.p.) injection and oral administration dramatically reduced both the weights (57%-100% inhibition) and volumes (78%-94% inhibition) of the tumors without any observed toxicity. These inhibitory effects were accompanied by mechanistic down-regulation of the protein levels of inflammatory enzymes (inducible nitric oxide synthase, iNOS
and cyclooxygenase-2, COX-2), metastasis (matrix metallopeptidase-2, MMP-2 and MMP-9), angiogenesis (vascular endothelial growth factor, VEGF), and proliferative molecules, as well as by the induction of apoptosis in prostate tumors. Our findings suggest that GL is an effective anti-cancer agent that may potentially serve as a novel therapeutic option for prostate cancer treatment.

[1505]
TÍTULO / TITLE: - Bladder cancer: Validating what we’ve got.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Zlotta AR
INSTITUCIÓN / INSTITUTION: - Department of Surgical Oncology (Urology), Mount Sinai Hospital, Toronto, ON.

[1506]
TÍTULO / TITLE: - Unilateral proptosis: an unusual presentation of prostatic carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Pouncey AL; Fox TP; Bryant CA
INSTITUCIÓN / INSTITUTION: - Oxford University, Oxford, UK.

[1507]
TÍTULO / TITLE: - Advanced urothelial carcinoma: moving the field forward.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Connexin 26 is Down-Regulated by KDM5B in the Progression of Bladder Cancer.

Connexin 26 (Cx26) expression is down-regulated and KDM5B (H3K4 demethylase) is up-regulated in the progression of bladder cancer, suggesting that Cx26 expression may be down-regulated by KDM5B in bladder cancer. To test the hypothesis, the HT1376 and T24 human bladder carcinoma cells were transfected with the plasmids pcDNA3.1-KDM5B, and caused the down-regulation of Cx26 expression. In contrast, the HT1376 and T24 cells transfected with the plasmids pTZU6+1-shRNA-KDM5B1 and pTZU6+1-shRNA-KDM5B2 caused the up-regulation of Cx26 expression. Immunohistochemistry and Spearman’s rank correlation analysis showed that the immunohistochemical expression of KDM5B and Cx26 was inversely related in bladder carcinoma tissues but no relationship in benign tissues. Taken together, these results indicate that KDM5B represses Cx26 expression in the bladder cancer development. Thus, a negative value to Cx26 immunohistochemical expression and a positive value to KDM5B immunohistochemical expression could be an ancillary diagnosis of primary bladder malignancy.

Plasma-seq: a novel strategy for metastatic prostate cancer analysis.

Plasma-seq: a novel strategy for metastatic prostate cancer analysis.
RESUMEN / SUMMARY: - Personalized genomics will only be useful for monitoring the prognosis of patients with cancer when it becomes much more cost-effective and quicker to apply. A recent study brings this closer to reality with the development of plasma-seq, a rapid, low-cost method that sequences the circulating DNA present in the peripheral blood of patients with cancer. The power of this technique is demonstrated with the examination of tumor genomes from patients with prostate cancer. See related research article: http://genomemedicine.com/content/5/4/30.

TÍTULO / TITLE: "Missing the target" in urothelial cancer.


AUTORES / AUTHORS: Dreicer R

INSTITUCIÓN / INSTITUTION: Department of Solid Tumor Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, Ohio, USA.

TÍTULO / TITLE: Comparison of 3 different postimplant dosimetry methods following permanent I prostate seed brachytherapy.


AUTORES / AUTHORS: Marcu LG; Gowda R

INSTITUCIÓN / INSTITUTION: Department of Medical Physics, Royal Adelaide Hospital, South Australia, Australia; Faculty of Science, University of Oradea, Romania; School of Chemistry and Physics, University of Adelaide, South Australia, Australia. Electronic address: loredana@marcunet.com.

RESUMEN / SUMMARY: Postimplant dosimetry (PID) after Iodine-125 (125I) implant of the prostate should offer a reliable qualitative assessment. So far, there is no consensus regarding the optimum PID method, though the latest literature is in favor of magnetic resonance imaging (MRI). This study aims to simultaneously compare 3 PID techniques: (1) MRI-computed tomography (CT) fusion; (2) ultrasound (US)-CT fusion; and (3) manual target delineation on CT. The study comprised 10 patients with prostate cancer. CT/MR scans with urinary catheters in place for PID were done either on day 0 or day 1 postimplantation. The main parameter evaluated and compared among methods was target D90. The results show that CT-based D90s are lower than US-CT D90s (median difference, -6.85%), whereas MR-CT PID gives higher D90 than US-CT PID (median difference, 4.25%). Manual contouring on CT images tends to overestimate the prostate volume compared with transrectal
ultrasound (TRUS) (median difference, 23.33%), whereas on US images the target is overestimated compared with MR-based contouring (median difference, 13.25%). Although there are certain differences among the results given by various PID techniques, the differences are statistically insignificant for this small group of patients. Any dosimetric comparison between 2 PID techniques should also account for the limitations of each technique, to allow for an accurate quantification of data. Given that PID after permanent radioactive seed implant is mandatory for quality assurance, any imaging method-based PID (MR-CT, US-CT, and CT) available in a radiotherapy department can be indicative of the quality of the procedure.

[1512]

TÍTULO / TITLE: - A New Algorithm for Integrated Analysis of miRNA-mRNA Interactions Based on Individual Classification Reveals Insights into Bladder Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Hecker N; Stephan C; Mollenkopf HJ; Jung K; Preissner R; Meyer HA
INSTITUCIÓN / INSTITUTION: - Center for Bioinformatics, University of Hamburg, Hamburg, Germany; Institute of Physiology, Charite - Universitätsmedizin Berlin, Berlin, Germany.
RESUMEN / SUMMARY: - BACKGROUND: MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression. It has been proposed that miRNAs play an important role in cancer development and progression. Their ability to affect multiple gene pathways by targeting various mRNAs makes them an interesting class of regulators. METHODOLOGY/PRINCIPAL FINDINGS: We have developed an algorithm, Classification based Analysis of Paired Expression data of RNA (CAPE RNA), which is capable of identifying altered miRNA-mRNA regulation between tissues samples that assigns interaction states to each sample without preexisting stratification of groups. The distribution of the assigned interaction states compared to given experimental groups is used to assess the quality of a predicted interaction. We demonstrate the applicability of our approach by analyzing urothelial carcinoma and normal bladder tissue samples derived from 24 patients. Using our approach, normal and tumor tissue samples as well as different stages of tumor progression were successfully stratified. Also, our results suggest interesting differentially regulated miRNA-mRNA interactions associated with bladder tumor progression. CONCLUSION/SIGNIFICANCE: The need for tools that allow an integrative analysis of microRNA and mRNA expression data has been
addressed. With this study, we provide an algorithm that emphasizes on the distribution of samples to rank differentially regulated miRNA-mRNA interactions. This is a new point of view compared to current approaches. From bootstrapping analysis, our ranking yields features that build strong classifiers. Further analysis reveals genes identified as differentially regulated by miRNAs to be enriched in cancer pathways, thus suggesting biologically interesting interactions.

[1513]

**TITULO / TITLE:** - Prostate Cancer Detection by Using Digital Rectal Examination: Contemporary Practice Patterns in the United States.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


- Enlace al texto completo (gratuito o de pago) 1016/j.clgc.2013.04.013

**AUTORES / AUTHORS:** - Tourville EA; Nguyen MM

**INSTITUCION / INSTITUTION:** - Division of Urology, College of Medicine, The University of Arizona, Tucson, AZ.

**RESUMEN / SUMMARY:** - BACKGROUND: Digital rectal examination (DRE) may play an important role as a secondary method of prostate cancer detection if prostate-specific antigen (PSA) screening decreases. Current practice patterns in the use of DRE are not well defined, and potential variations in its use among different subgroups of men are unclear. MATERIALS AND METHODS: The Behavioral Risk Factor Surveillance System was examined for the year 2010. All men aged 40 years old or older were asked if they ever had a rectal examination to check their prostate and the date of their last examination. Men who reported having had a DRE within the past 12 months were considered up to date. The proportion of men who reported having had a DRE and independent demographic and socioeconomic predictors for having had a DRE were determined. RESULTS: A total of 110,661 respondents were included: 72.2% of respondents reported ever having had a DRE; 36.8% had had a DRE within the past year, and 49.7% within the past 2 years. On multivariate analysis for reporting having an up-to-date DRE, older men, those with higher body mass index, and those of black race were more likely to have an up-to-date DRE. Asian or Hispanic race, divorced or widowed marital status, lower education, lower income, and lack of health insurance were independently associated with being less likely to have an up-to-date DRE. CONCLUSIONS: Of American men, 36.8% reported having an up-to-date DRE within the past year and 49.7% of men within the past 2 years. Demographic and socioeconomic characteristics were strongly associated with the likelihood of having an up-to-date DRE.

[1514]
Penile nodule with inguinal lymphadenopathy: Prostatic adenocarcinoma masquerading as penile cancer.

Although anatomically the penis is closely related to the prostate, penile metastasis from prostate cancer is an uncommon phenomenon. These patients usually present late in the course of the disease with widespread metastasis. We report a patient who presented with a penile mass and inguinal lymphadenopathy. He was clinically diagnosed as a case of penile cancer but the penile mass as well as the inguinal lymphadenopathy was subsequently diagnosed to be metastases from carcinoma of the prostate.

Renal cell carcinoma metastatic to thyroid gland, presenting like anaplastic carcinoma of thyroid.

Background. Renal cell carcinoma (RCC) has unpredictable and diverse behavior. The classic triad of hematuria, loin pain, and abdominal mass is uncommon. At time of diagnosis, 25%-30% of patients are found to have metastases. Bones, lungs, liver, and brain are the frequent sites of metastases. RCC with metastasis to the head and neck region and thyroid gland is the rarest manifestation and anaplastic carcinoma behaving metastatic thyroid mass is an extremely rare presentation of RCC. Case Presentation. A 56-year-old Saudi man with past history of right radical nephrectomy 5 years back presented with 3 months history of rapid increasing neck mass with dysphagia, presenting like anaplastic thyroid carcinoma. Tru-cut biopsy turned out to be metastatic renal cell carcinoma. Patient was treated with radiation therapy 30 Gy in 10 fractions to mass. Patient died 4 months after the discovery of anaplastic thyroid looking metastasis. Conclusion. Rapidly progressing thyroid metastases secondary to RCC are rare and found often
unresectable which are not amenable to surgery. Palliative radiotherapy can be considered for such patients.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Meijer HJ; Debats OA; Th van Lin EN; van Vulpen M; Witjes JA; Oyen WJ; Barentsz JO; Kaanders JH
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Radboud University Nijmegen Medical Centre, P. O. Box 9101, 6500 HB Nijmegen, The Netherlands.
RESUMEN / SUMMARY: - Controversy surrounds the benefit of whole pelvis radiotherapy (WPRT) over prostate-only radiotherapy (PORT) for intermediate-risk and high-risk patients with prostate cancer. In the PSA screening era, two large randomized trials as well as multiple retrospective studies comparing WPRT with PORT have been performed, albeit with contradictory results. Data regarding the use of WPRT in patients with biochemical recurrence after prostatectomy are scarce. As a consequence, the practice of WPRT varies worldwide. Advanced highly accurate imaging methods for the detection of lymph node metastases in patients with prostate cancer have been developed, such as PET, single photon emission computed tomography (SPECT), diffusion-weighted MRI and magnetic resonance lymphography (MRL). The use of these new imaging methods might improve nodal irradiation, as they can be used not only for selection of patients, but also for accurately determining the target volume to reduce geographical miss. Furthermore, these new techniques can enable dose escalation to involved lymph nodes.

[1517] TÍTULO / TITLE: - Prostate cancer: TMPRSS2:ERG-the root of the problem?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Clyne M

[1518] TÍTULO / TITLE: - Prostate cancer: Turning the COGS-23 new susceptibility loci identified.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
TÍTULO / TITLE: - T(2)-weighted combined with diffusion-weighted images for evaluating prostatic transition zone tumors at 3 Tesla.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Ren J; Yang Y; Zhang J; Xu J; Liu Y; Wei M; Ge Y; Huan Y; Larson AC; Zhang Z

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Xijing Hospital, Fourth Military Medical University, 15 Chang Le Western Road, Xi'an 710032, China.

RESUMEN / SUMMARY: - AIM: We hypothesize that the combination of T(2)-weighted (T(2)W) MRI with diffusion-weighted imaging (DWI) methods provides a powerful clinical application for the differential diagnosis of prostate cancer and benign lesion in the prostatic transition zone (TZ). METHODS: This retrospective study included 113 patients who were diagnosed with TZ lesions by MRI. The apparent diffusion coefficient values were compared between biopsy-proven benign and malignant lesions. RESULTS: The apparent diffusion coefficient values for the malignant nodules were significantly lower than those of the benign nodules. The area under the curve values for T(2)W imaging combined with DWI and T(2)W imaging alone were 0.991 and 0.884, respectively. CONCLUSION: T(2)W combined with DWI provides a powerful tool for noninvasive differentiation between malignant and benign prostatic hyperplasia nodules in the prostatic TZ.

[1520]

TÍTULO / TITLE: - Comparison of low and intermediate source strengths for prostate brachytherapy implants.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Usmani N; Martell K; Ghosh S; Moore H; Pervez N; Pedersen J; Yee D; Murtha A; Amanie J; Sloboda R

INSTITUCIÓN / INSTITUTION: - Division of Radiation Oncology, Cross Cancer Institute, Edmonton, Alberta, Canada; Department of Oncology, University of
RESUMEN / SUMMARY: - PURPOSE: To compare the implant quality and clinical outcomes for patients treated with low and intermediate strength 125I seeds in prostate brachytherapy implants. METHODS AND MATERIALS: This retrospective review included 390 consecutive patients treated with prostate brachytherapy from 1999 to 2006. The first 142 patients were implanted with source strengths lower than 0.415U (0.327mCi), with the subsequent 248 patients implanted with source strengths higher than 0.493U (0.388mCi). Clinical, dosimetric, toxicity, and outcome data were compared between these two cohorts of patients. RESULTS: Despite having similar prostate volumes, fewer sources (median, 95 vs. 113; p<0.0001) and fewer needles (median, 23 vs. 29; p<0.0001) were implanted in the intermediate strength cohort. The postimplant dosimetry demonstrated better quality implants in patients treated with intermediate strength sources (median D90, 160.0Gy vs. 139.6Gy; p<0.0001), with greater dose inhomogeneity identified in the intermediate strength cohort of patients. A higher incidence of late rectal toxicity was identified in patients treated with intermediate strength sources despite lower rectal doses in this cohort. The biochemical relapse-free survival, prostate cancer survival, and overall survival were not significantly different between the two cohorts. CONCLUSIONS: The transition from low to intermediate strength sources has led to fewer resources being used and improved postoperative dosimetry. Although there were more rectal complications identified in the intermediate strength cohort of patients in this analysis, there were no other significantly worse clinical or biochemical outcomes for patients implanted with intermediate strength sources.

[1521]


RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Emonds KM; Swinnen JV; Lerut E; Koole M; Mortelmans L; Mottaghy FM

INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, University Hospitals Leuven, Leuven 3000, Belgium. fmottaghy@ukaachen.de.

RESUMEN / SUMMARY: - BACKGROUND: Androgen deprivation (AD) is generally used as a first-line palliative treatment in prostate cancer (PCA) patients with rising prostate-specific antigen (PSA) after primary therapy. To acquire an accurate detection of tumour viability following AD with positron
emission tomography (PET), an androgen-independent uptake of tracers would be advantageous. Several metabolic PET tracers are employed for detecting recurrent PCa. We evaluated the effect of AD on the uptake of 2-deoxy-2-[18F]fluoro-d-glucose ([18F]FDG), [11C]choline and [11C]acetate in vivo.

METHODS: An [18F]FDG, [11C]choline and [11C]acetate baseline micro(mu)PET/mu computed tomography (CT) scan was subsequently performed in xenografts of androgen-sensitive (LAPC-4) and androgen-independent (22Rv1) tumours in nude mice. An untreated control group was compared to a surgical castration group, i.e. androgen-deprived group. muPET/muCT imaging with the above-mentioned tracers was repeated 5 days after the start of treatment. The percentage change of SUVmax and SUVmeanTH in the tumours was calculated. RESULTS: AD did not significantly affect the uptake of [18F]FDG and [11C]choline in LAPC-4 tumours as compared with the uptake of both tracers in untreated tumours. In control 22Rv1 tumours, [11C]choline and [18F]FDG uptake increased over time. However, compared with the uptake in control tumours, AD significantly decreased the uptake of [11C]choline and tended to decrease [18F]FDG uptake. [11C]acetate uptake remained unaffected by AD in both PCa xenograft models. CONCLUSIONS: [18F]FDG and especially [11C]choline PET, which is currently used for the detection of recurrent PCa, could miss or underestimate the presence of local recurrent PCa following AD therapy. [11C]acetate uptake occurs independently of androgens and thus may be more favourable for detecting tumour viability during or following AD.

[1522]

TITULO / TITLE: Fibroepithelial polyp of the glans penis due to pad use for urinary incontinence.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Kumsar S; Saglam HS; Kose O; Budak S; Adsan O
INSTITUCIÓN / INSTITUTION: Sakarya Education and Training Hospital, Sakarya, Turkey;

RESUMEN / SUMMARY: A 78-year-old man was admitted to our urology polyclinic with painless penile mass. The lesion was 3.5 cm in size on the ventral aspect of the penis. He had been using a pad for urinary incontinence for 10 months and said that the lesion had been increasing in size for past 3 months. He underwent a wide local excision under local anesthesia. The histopathologic diagnosis was fibroepithelial polyp. A fibroepithelial polyp of the penis is very rare and strongly linked to long-term condom catheter use. We present a case of fibroepithelial polyp of the glans which is not associated with condom catheter use.

RESUMEN / SUMMARY: - Multilocular cystic renal cell carcinoma (MCRCC) is an uncommon subtype of clear cell renal cell carcinoma that appears to have a favourable prognosis. Literature reports a very low incidence of 1-2% of MCRCC among the renal neoplasms. The first such reported case was in 1957 by Robinson. In 1998, Eble et al suggested following diagnostic criterion for MCRCC: (1) an expansile mass surrounded by a fibrous capsule; (2) interior of tumour entirely composed of cysts and septa with no expansile nodule or solid component confined to more than 10% of entire tumour and (3) septa containing aggregates of clear epithelial cells. We report a case of MCRCC in a 60-year-old male patient who presented with abdominal lump and after suspicion of renal malignancy underwent nephrectomy. The patient was perfectly well till last follow-up of 3 months postoperatively.

AUTORES / AUTHORS: - Singhai A; Babu S; Verma N; Singh V

INSTITUCIÓN / INSTITUTION: - Department of Pathology, King George’s Medical University, Lucknow, Uttar Pradesh, India. atinsinghai@yahoo.com

[1524]

TÍTULO / TITLE: - Sarcomatoid carcinoma of the prostate.

RESUMEN / SUMMARY: - Sarcomatoid carcinoma of the prostate is among the rarest malignant neoplasm types and has been well known for its aggressive clinical course. Patient was admitted with the symptoms of lower urinary tract. Transurethral resection of prostate (TUR-P) was carried out. Revealing Gleason 5 + 3 = 8 prostate adenocarcinoma in TUR-P material. Thereby, a Radical Prostatectomy procedure was planned. In operation, frozen examination revealed adenocarcinoma metastasis to the obturator lymph node. The
operation was terminated. In the postoperative 3rd month, the patient was re-admitted with acute urinary system symptoms. A cystoscopy performed and complete resection of the mass was performed. The pathological examination reported that the tumor was compatible with undifferentiated adenocarcinoma owing to presence of poorly differentiated tumoral cells and detection of adenocarcinoma in a relatively small (<1%) focus. 4 month after the operation, the patient underwent another cystoscopic examination which revealed the prostatic lounge and most of the bladder lumen to be filled with tumoral tissue. The tumoral tissues was resected incompletely. This material was diagnosed to be “Sarcomatoid Malignant Tumor” upon the new evidences of progressive dedifferentiation and predominant sarcomatoid appearance, compared with the former TUR-P materials. Subsequent PET-CT scan depicted multiple metastasis. The patient was referred to oncology department. In conclusion, sarcomatoid carcinoma is a malignant variant that brings along diagnostic and treatment difficulties.

[1525]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Cosset JM; Cathelineau X; Wakil G; Pierrat N; Quenzer O; Prapotnich D; Barret E; Rozet F; Galiano M; Vallancien G
INSTITUCIÓN / INSTITUTION: - Department of Oncology/Radiotherapy, Institut Curie, Paris, France; Department of Urology, Institut Mutualiste Montsouris, Paris, France. Electronic address: jean-marc.cosset@curie.net.
RESUMEN / SUMMARY: - PURPOSE: To evaluate the feasibility and the early toxicity of focal brachytherapy in highly selected localized prostate cancer patients. METHODS AND MATERIALS: Twenty-one patients underwent a focal brachytherapy between February 2010 and March 2012, representing 3.7% of the cases treated by our group during this period. Patient selection was based on (at least) two series of prostate biopsies and a high-resolution MRI. Only patients with very limited and localized tumors, according to strict criteria, were selected for the procedure. The technique used a real-time procedure with the implantation of free 125I seeds and dynamic dose calculation. The prescribed dose for the focal volume was 145Gy. RESULTS: The treated volume corresponded to a mean value of 34% of the total prostatic volume (range, 20-48%). For the focal volume, the mean D90 and V100 was 183.2Gy (range, 176-188Gy) and 99.3% (range, 98.8-100%), respectively. The technique was performed in an hour and a half. When compared with a previous cohort treated
by whole-prostate brachytherapy, urinary toxicity (International Prostate Symptom Score) was borderline reduced (p = 0.04) at 6 months only, whereas the recovery of the International Index of Erectile Function 5 was better (p = 0.014). The International Continence Score was nil in almost all cases as well as rectal toxicity. CONCLUSION: Focal treatment by brachytherapy is easily feasible with little acute toxicity. Further investigation is needed to assess the results in terms of tumor control and long-term toxicity.
**RESUMEN / SUMMARY:** Treatment for advanced prostate cancer has and will continue to grow increasingly complex, owing to the introduction of multiple new therapeutic approaches with the potential to substantially improve outcomes for this disease. Agents that modulate the patient's immune system to fight prostate cancer - immunotherapeutics - are among the most exciting of these new approaches. The addition of antigen-specific immunotherapy to the treatment of castration-resistant prostate cancer (CRPC) has paved the way for additional research that seeks to augment the activity of the immune system itself. The monoclonal antibody ipilimumab, approved in over 40 countries to treat advanced melanoma and currently under phase 2 and 3 investigation in prostate cancer, is thought to act by augmenting immune responses to tumors through blockade of cytotoxic T-lymphocyte antigen 4, an inhibitory immune checkpoint molecule. Ipilimumab has been studied in seven phase 1 and 2 clinical trials that evaluated various doses, schedules, and combinations across the spectrum of patients with advanced prostate cancer. The CRPC studies of ipilimumab to date suggest that the agent is active in prostate cancer as monotherapy or in combination with radiotherapy, docetaxel, or other immunotherapeutics, and that the adverse event profile is as expected given the safety data in advanced melanoma. The ongoing phase 3 program will further characterize the risk/benefit profile of ipilimumab in chemotherapy-naive and -pretreated CRPC.

[1529]
**TÍTULO / TITLE:** Bladder cancer: Biomarker panel predicts recurrence after radical cystectomy.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.95
**AUTORES / AUTHORS:** Payton S

[1530]
**TÍTULO / TITLE:** Transvesical enucleation of multiple leiomyoma of bladder and urethra.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary
  ●●Enlace al texto completo (gratuito o de pago) 5812/numonthly.5122
**AUTORES / AUTHORS:** Ghadian A; Hoseini SY
**INSTITUCIÓN / INSTITUTION:** Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, IR Iran.
RESUMEN / SUMMARY: - Aunque la leiomioma de vejiga es raro, es el tumor benigno más frecuente no epitelial de la vejiga. Los síntomas y el tratamiento dependen de la ubicación y el tamaño de la lesión. La opción terapéutica más común es una enucleación total o parcial de la vejiga, aunque en casos demostrados por biopsia, el tratamiento de espera puede ser una opción. La cirugía debería considerarse si el tumor crece o se observan síntomas. La etiología del leiomioma de vejiga es desconocida. El leiomioma uterino es conocido como reactivivo a la estrogén. Las mujeres premenopáusicas son prevalentes en la cuarta década.

[1531]

TÍTULO / TITLE: - Evidence for a Pro-Proliferative Feedback Loop in Prostate Cancer: The Role of Epac1 and COX-2-Dependent Pathways.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Misra UK; Pizzo SV

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Duke University Medical Center, Durham, North Carolina, United States of America.

RESUMEN / SUMMARY: - OBJECTIVE: In human prostate cancer cells, a selective Epac agonist, 8-CPT-2Me-cAMP, upregulates cell proliferation and survival via activation of Ras-MAPK and PI 3-kinase-Akt-mTOR signaling cascades. Here we examine the role of inflammatory mediators in Epac1-induced cellular proliferation by determining the expression of the pro-inflammatory markers p-cPLA2, COX-2, and PGE2 in prostate cancer cells treated with 8-CPT-2Me-cAMP. METHODS: We employed inhibitors of COX-2, mTORC1, and mTORC2 to probe cyclic AMP-dependent pathways in human prostate cancer cells. RNAi targeting Epac1, Raptor, and Rictor was also employed in these studies. RESULTS: 8-CPT-2Me-cAMP treatment caused a 2.2-5-fold increase of p-cPLA2(S505), COX-2, and PGE2 levels in human prostate cancer cell lines. Pretreatment of cells with the COX-2 inhibitor SC-58125 or the EP4 antagonist AH-23848, or with an inhibitor of mTORC1 and mTORC2, Torin1, significantly reduced the Epac1-dependent increase of p-cPLA2 and COX-2, p-S6-kinase(T389), and p-AKT(S473). In addition, Epac1-induced protein and DNA synthesis were greatly reduced upon pretreatment of cells with either COX-2, EP4, or mTOR inhibitors. Transfection of prostate cancer cells with Epac1 dsRNA, Raptor dsRNA, or Rictor dsRNA profoundly reduced Epac1-dependent increases in p-cPLA2 and COX-2. CONCLUSION: We show that Epac1, a downstream effector of cAMP, functions as a pro-inflammatory modulator in prostate cancer cells and promotes cell proliferation and survival by upregulating Ras-MAPK, and PI 3-kinase-Akt-mTOR signaling.

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Active surveillance of small renal masses.

The increased diagnosis of small renal masses (SRMs) poses the challenge of how best to manage patients with tumours that are not likely to progress and cause death during their lifetime. Concerns regarding overdiagnosis and overtreatment of patients with low-risk or indolent disease has led to the introduction of active surveillance as an alternative to immediate intervention in select candidates. However, differentiating between benign or low-grade lesions and high-grade aggressive phenotypes is difficult. Renal biopsy, radiographic assessment, and clinical nomograms have been used before surgery to evaluate the probability of whether an SRM will exhibit characteristics of an aggressive cancer. SRM growth trends have been studied over periods of observation but no characteristics have been found to correlate with aggressive growth kinetics. Stratification of patients with SRMs according to risk status is crucial when considering whether active surveillance might be an appropriate treatment option. Factors that should be taken into account include comorbidities, a history of malignancy, pre-existing chronic kidney disease, life expectancy and patient preference. Standardized active surveillance protocols are currently lacking, and clinical trials designed to randomize patients with SRMs to receive either active surveillance or immediate treatment are sorely needed to address the existing evidence gap.

Small renal masses: Jury still out on robotic partial nephrectomy.

Circulating MicroRNAs as Biomarkers of Prostate Cancer: The State of Play.
ENLACE AL TEXTO COMPLETO (GRATUITO O DE PAGO) 1155/2013/539680

TÍTULO / TITLE: - A preclinical xenograft model of prostate cancer using human tumors.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Lawrence MG; Taylor RA; Toivanen R; Pedersen J; Norden S; Pook DW; Frydenberg M; Papargiris MM; Niranjan B; Richards MG; Wang H; Collins AT; Maitland NJ; Risbridger GP

INSTITUCIÓN / INSTITUTION: - Department of Anatomy and Developmental Biology, Monash University, Clayton, Victoria, Australia.

RESUMEN / SUMMARY: - Most cases of prostate cancer are now diagnosed as moderate-grade localized disease. These tumor specimens are important tools in the discovery and translation of prostate cancer research; however, unlike more advanced tumors, they are notoriously difficult to grow in the laboratory. We developed a system for efficiently xenografting localized human prostate cancer tissue, and we adapted this protocol to study the interactions between the specific subsets of epithelial and stromal cells. Fresh prostate tissues or isolated epithelial cells are recombined with mouse seminal vesicle mesenchyme (SVM) and grafted under the renal capsule of immunodeficient mice for optimum growth and survival. Alternatively, mouse mesenchyme can be replaced with human prostate fibroblasts in order to determine their
contribution to tumor progression. Grafts can be grown for several months to determine the effectiveness of novel therapeutic compounds when administered to host mice, thereby paving the way for personalizing the treatment of individual prostate cancers.

[1536]

**TÍTULO / TITLE:** - Monitor unit optimization in RapidArc plans for prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Clemente S; Cozzolino M; Chiumento C; Fiorentino A; Caivano R; Fusco V

**INSTITUCIÓN / INSTITUTION:** - IRCCS CROB. clemente_stefania@libero.it

**RESUMEN / SUMMARY:** - Intensity-modulated radiation therapy (IMRT) has become a standard treatment for prostate cancer based on the superior sparing of the bladder, rectum, and other surrounding normal tissues compared to three-dimensional conformal radiotherapy, despite the longer delivery time and the increased number of monitor units (MU). The novel RapidArc technique represents a further step forward because of the lower number of MUs per fraction and the shorter delivery time, compared to IMRT. This paper refers to MU optimization in RA plans for prostate cancer, using a tool incorporated in Varian TPS Eclipse. The goal was to get the lowest MU RA plan for each patient, keeping a well-defined level of PTV coverage and OAR sparing. Seven prostate RA plans (RA MU-Optimized) were retrospectively generated using the MU optimization tool in Varian Eclipse TPS. Dosimetric outcome and nontarget tissue sparing were, compared to those of RA clinical plans (RA Clinical) used to treat patients. Compared to RA Clinical, RA MU-Optimized plans resulted in an about 28% (p = 0.018) reduction in MU. The total integral dose (ID) to each nontarget tissue (but not the penile bulb) showed a consistent average relative reduction, statistically significant only for the femoral heads. Within the intermediate dose region (40-60 Gy), ID reductions (4%-17% p < 0.05) were found for the rectum, while a slight but significant (0.4%-0.9%, p < 0.05) higher ID was found for the whole body. Among the remaining data, the mean dose to the bladder was also reduced (-12%, p = 0.028). Plans using MU optimization are clinically applicable and more MU efficient, ameliorating the exposure of the rectum and the bladder to intermediate doses.

[1537]

**TÍTULO / TITLE:** - Discovery of a Selective Irreversible BMX Inhibitor for Prostate Cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

BMX is a member of the TEC family of nonreceptor tyrosine kinases. We have used structure-based drug design in conjunction with kinome profiling to develop a potent, selective, and irreversible BMX kinase inhibitor, BMX-IN-1, which covalently modifies Cys496. BMX-IN-1 inhibits the proliferation of Tel-BMX-transformed Ba/F3 cells at two digit nanomolar concentrations but requires single digit micromolar concentrations to inhibit the proliferation of prostate cancer cell lines. Using a combinatorial kinase inhibitor screening strategy, we discovered that the allosteric Akt inhibitor, MK2206, is able to potentiate BMX inhibitor’s antiproliferation efficacy against prostate cancer cells.

[1538]
TÍTULO / TITLE: Pyogenic renal abscess masquerading as malignancy.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Baid M; De U; Kar M
INSTITUCIÓN / INSTITUTION: Department of Surgery, Medical College, Kolkata, India. E-mail: drmayankbaid@gmail.com.

[1539]
TÍTULO / TITLE: Estrogen-Dependent Dynamic Profile of eNOS-DNA Associations in Prostate Cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Nanni S; Aiello A; Re A; Guffanti A; Benvenuti V; Colussi C; Castro-Vega LJ; Felsani A; Londono-Vallejo A; Capogrossi MC; Bacchetti S; Gaetano C; Pontecorvi A; Farsetti A
INSTITUCIÓN / INSTITUTION: Department of Experimental Oncology, National Cancer Institute Regina Elena, Rome, Italy; Medical Pathology Institute, Catholic University, Rome, Italy.
RESUMEN / SUMMARY: In previous work we have documented the nuclear translocation of endothelial NOS (eNOS) and its participation in combinatorial
complexes with Estrogen Receptor Beta (ERβ) and Hypoxia Inducible Factors (HIFs) that determine localized chromatin remodeling in response to estrogen (E2) and hypoxia stimuli, resulting in transcriptional regulation of genes associated with adverse prognosis in prostate cancer (PCa). To explore the role of nuclear eNOS in the acquisition of aggressive phenotype in PCa, we performed ChIP-Seq on chromatin-associated eNOS from cells from a primary tumor with poor outcome and from metastatic LNCaP cells. We found that: 1. the eNOS-bound regions (peaks) are widely distributed across the genome encompassing multiple transcription factors binding sites, including Estrogen Response Elements. 2. E2 increased the number of peaks, indicating hormone-dependent eNOS re-localization. 3. Peak distribution was similar with/without E2 with approximately 55% of them in extragenic DNA regions and an intriguing involvement of the 5’ domain of several miRs deregulated in PCa. Numerous potentially novel eNOS-targeted genes have been identified suggesting that eNOS participates in the regulation of large gene sets. The parallel finding of downregulation of a cluster of miRs, including miR-34, in PCa cells associated with poor outcome led us to unveil a molecular link between eNOS and SIRT1, an epigenetic regulator of aging and tumorigenicity, negatively regulated by miR-34 and in turn activating eNOS. E2 potentiates miR-34 downregulation thus enhancing SIRT1 expression, depicting a novel eNOS/SIRT1 interplay fine-tuned by E2-activated ER signaling, and suggesting that eNOS may play an important role in aggressive PCa.

[TÍTULO / TITLE]: - Inherently multimodal nanoparticle-driven tracking and real-time delineation of orthotopic prostate tumors and micrometastases.

[RESUMEN / SUMMARY]: - Enlace al Resumen / Link to its Summary


[ENLACE AL TEXTO COMPLETO (GRATUITO O DE PAGO)]: 1021/nn400669r

[AUTORES / AUTHORS]: - Liu TW; Macdonald TD; Jin CS; Gold JM; Bristow RG; Wilson BC; Zheng G

[INSTITUCION / INSTITUTION]: - Ontario Cancer Institute, Campbell Family Institute for Cancer Research and Techna Institute , UHN, 610 University Avenue, Toronto, ON Canada M5G 2M9.

[RESUMEN / SUMMARY]: - Prostate cancer is the most common cancer among men and the second cause of male cancer-related deaths. There are currently three critical needs in prostate cancer imaging to personalize cancer treatment: (1) accurate intraprostatic imaging for multiple foci and extra-capsular extent; (2) monitoring local and systemic treatment response and predicting recurrence; and (3) more sensitive imaging of occult prostate cancer bone metastases. Recently, our lab developed porphysomes, inherently multimodal, all-organic nanoparticles with flexible and robust radiochemistry. Herein, we validate the
first in vivo application of (64)Cu-porphysomes in clinically relevant orthotopic prostate and bony metastatic cancer models. We demonstrate clear multimodal delineation of orthotopic tumors on both the macro- and the microscopic scales (using both PET and fluorescence) and sensitively detected small bony metastases (<2 mm). The unique and multifaceted properties of porphysomes offers a promising all-in-one prostate cancer imaging agent for tumor detection and treatment response/recurrence monitoring using both radionuclide- and photonic-based strategies.

[1541] **TÍTULO / TITLE:** - Spermatic cord metastasis as early manifestation of small bowel adenocarcinoma.  
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)  
**AUTORES / AUTHORS:** - Valizadeh N; Oskuie AE; Tehranchi A  
**INSTITUCIÓN / INSTITUTION:** - Assistant Professor of Hematology/Medical Oncology, Urmia University of Medical Sciences, Urmia, Iran.  
**RESUMEN / SUMMARY:** - Malignant tumors of the spermatic cord are rare. There are a few case reports on spermatic cord metastasis from colonic, gastric, pancreas, and prostatic cancer. Here, we report a 36-year-old man with brucellosis presenting with spermatic cord metastasis as early manifestation of small bowel adenocarcinoma.

[1542] **TÍTULO / TITLE:** - Perlman Syndrome: Overgrowth, Wilms Tumor Predisposition and DIS3L2.  
**RESUMEN / SUMMARY:** - [Enlace al Resumen / Link to its Summary](#)  
**AUTORES / AUTHORS:** - Morris MR; Astuti D; Maher ER  
**RESUMEN / SUMMARY:** - Perlman syndrome is a rare autosomal recessively inherited congenital overgrowth syndrome characterized by polyhydramnios, macrosomia, characteristic facial dysmorphology, renal dysplasia and nephroblastomatosis and multiple congenital anomalies. Perlman syndrome is associated with high neonatal mortality and, survivors have developmental delay and a high risk of Wilms tumor. Recently a Perlman syndrome locus was mapped to chromosome 2q37 and homozygous or compound heterozygous mutations were characterized in DIS3L2. The DIS3L2 gene product has ribonuclease activity and homology to the DIS3 component of the RNA
exosome. It has been postulated that the clinical features of Perlman syndrome result from disordered RNA metabolism and, though the precise targets of DIS3L2 have yet to be characterized, in cellular models DIS3L2 knockdown is associated with abnormalities of cell growth and division. © 2013 Wiley Periodicals, Inc.

[1543]
**TITULO / TITLE:** - Intraluminal urethral brachytherapy for recurrence of transitional cell carcinoma of urinary bladder in urethral stump.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Chakrabarti B; Ghorai S; Ray SB; Kar SK

**INSTITUCIÓN / INSTITUTION:** - Institute of Post-Graduate Medical Education and Research, Kolkata, India.

**RESUMEN / SUMMARY:** - We report a unique case of successfully performed intraluminal brachytherapy for low volume urethral mucosal recurrence of transitional cell carcinoma urinary bladder, initially treated by transurethral resection of bladder tumor, followed by radical cystectomy. Since the patient was unwilling to undergo any other operational interventions, intraluminal brachytherapy of urethra was attempted. Fluroscopy guided intraluminal HDR brachytherapy using Lumencath® catheter under local anesthesia, and remote afterloading system (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) was performed. A fraction dose of 7 Gy in seven weekly fractions was prescribed at 0.5 cm from the single applicator. The result was promising in terms of local control and symptomatic relief. Therefore, intraluminal brachytherapy in low volume superficial local disease in urethra may play a potential role, and should be applied when repeated surgery is not feasible due to technical or medical reasons.

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[1544]
**TITULO / TITLE:** - Zoledronic acid in genitourinary cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

**REVISTA / JOURNAL:** - Clin Transl Oncol. 2013 Apr 25.

**AUTORES / AUTHORS:** - Climent MA; Anido U; Mendez-Vidal MJ; Puente J

**INSTITUCIÓN / INSTITUTION:** - Servicio de Oncologia Medica, Instituto Valenciano de Oncologia (IVO), C/Beltran Baguena, 8, 46009, Valencia, España, macliment@ivo.org.

**RESUMEN / SUMMARY:** - Bone metastases are a common complication of advanced prostate cancer and while they are less common in non-prostate
genitourinary (GU) malignances, they have been reported in up to 35% of patients with advanced renal cell carcinoma and bladder cancer. Furthermore, they may occur in more than two-thirds of those patients with bladder cancer who develop distant metastases. In the absence of bone-targeted therapies, approximately 50% of all patients with metastatic bone disease from GU cancers experience at least one skeletal-related event within their lifetime. Zoledronic acid is a bisphosphonate that has been shown to delay or prevent the development of skeletal complications in patients with bone metastases and reduce bone pain in these patients. Furthermore, zoledronic acid has also demonstrated the ability to prevent osteopenia, which may occur with the prolonged use of some pharmacological interventions in patients with cancer.

[1545]

TITULO / TITLE: - Prostate cancer overdiagnosis and overtreatment.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

- Enlace al texto completo (gratuito o de pago) 1097/MED.0b013e328360332a

AUTORES / AUTHORS: - Klotz L
INSTITUCIÓN / INSTITUTION: - University of Toronto, Sunnybrook Health Sciences Centre, 2075 Bayview Ave MG 408, Toronto, Ontario, Canada.

RESUMEN / SUMMARY: - PURPOSE OF REVIEW: To summarize the evidence, now extensive, that efforts to reduce prostate cancer mortality by screening and early detection result in overdiagnosis of disease that is clinically insignificant, and would never have been diagnosed in the patient’s lifetime in the absence of screening. Overdiagnosis may result in overtreatment, which in the case of prostate cancer often carries significant, long-term quality-of-life effects. The review also addresses the solutions to the problem of overdiagnosis and overtreatment, and summarizes the outcomes of these approaches. RECENT FINDINGS: Screening for prostate cancer has been demonstrated to reduce mortality, although with a high number needed to treat. One approach to this problem is to offer patients with favorable risk disease an initial conservative approach, with close monitoring and treatment for those patients who are reclassified as higher risk over time. Much preclinical data indicates that Gleason 6 prostate cancer does not carry the hallmarks of malignancy. However, a number of recent studies have demonstrated that in patients diagnosed with favorable risk prostate cancer (Gleason 6 or less, prostate-specific antigen <10), about 30% will harbor higher grade cancer and benefit from treatment. These patients are identifiable by a combination of repeat biopsy, serial prostate-specific antigen, and in borderline cases, multiparametric MRI. SUMMARY: Active surveillance is a powerful solution to the problem of overdiagnosis and overtreatment associated with screening for prostate cancer.
For the 40-50% of patients with favorable risk prostate cancer, it offers the benefit of personalized medicine, avoiding treatment and related quality-of-life effects altogether in the majority, and providing definitive management for the minority who are reclassified with higher risk disease over time.

[1546]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Spiess PE; Horenblas S; Pagliaro LC; Biagioli MC; Crook J; Clark PE; Greenberg RE; Ercole CE
INSTITUCIÓN / INSTITUTION: - From the aDepartment of Genitourinary Oncology, Moffitt Cancer Center, Tampa, Florida; bDepartment of Urology, Netherlands Cancer Institute, Amsterdam, The Netherlands; cDepartment of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas; dDepartment of Radiation Oncology, Division of Brachytherapy, Moffitt Cancer Center, Tampa, Florida; eUniversity of British Columbia, BCCA Center for the Southern Interior, British Columbia, Canada; fDepartment of Urology, Vanderbilt University Medical Center, Nashville, Tennessee; and gDepartment of Urology, Fox Chase Cancer Center, Philadelphia, Pennsylvania.
RESUMEN / SUMMARY: - This review highlights the significant advances made in the diagnosis and management of penile cancer. This often-aggressive tumor phenotype has been characterized by its poor prognosis, mostly attributable to its late presentation and heterogeneity of surgical care because of the paucity of cases treated at most centers. Recent advances in understanding of the risk factors predisposing to penile cancer, including its association with the human papilloma virus (HPV), have brought forth the socioeconomic concept of HPV vaccination in certain high-risk populations and countries, which remains highly debated. The management of penile cancer has evolved in recent years with the adoption of penile-sparing and minimally invasive surgical approaches to the inguinal lymph nodes, which are a frequent site of regional spread for this malignancy. Lastly, this review highlights the importance of adopting a multimodal approach consisting of neoadjuvant systemic chemotherapy followed by consolidative surgical resection in patients presenting with bulky/locally advanced nodal metastases from penile cancer.

[1547]
TÍTULO / TITLE: - Prostate carcinoma presenting with bulky mediastinal and cervical lymphadenopathy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
The emerging role of high-dose-rate (HDR) brachytherapy as monotherapy for prostate cancer.

In addition to the intrinsic advantages of brachytherapy, including radiation dose concentration to the tumor and rapid dose fall-off at the surrounding normal tissue, HDR brachytherapy can yield a more homogeneous and conformal dose distribution through image-based decisions for source dwell positions and by optimization of individual source dwell times. Indication can be extended even to T3a/b or a part of T4 tumors because the applicators can be positioned at the extracapsular lesion, into the seminal vesicles, and/or into the bladder, without any risk of source migration or dropping out. Unlike external beam radiotherapy, with HDR brachytherapy inter-/intra-fraction organ motion is not problematic. However, HDR monotherapy requires patients to stay in bed for 1-4 days during hospitalization, even though the actual overall treatment time is short. Recent findings that the alpha/beta value for prostate cancer is less than that for the surrounding late-responding normal tissue has made hypofractionation attractive, and HDR monotherapy can maximize this advantage of hypofractionation. Research on HDR monotherapy is accelerating, with a growing number of publications reporting excellent preliminary clinical results due to the high ‘biologically effective dose (BED)’ of >200 Gy. Moreover, the findings obtained for HDR monotherapy as an early model of extreme hypofractionation tend to be applied to other radiotherapy techniques such as stereotactic radiotherapy. All these developments point to the emerging role of HDR brachytherapy as monotherapy for prostate cancer.
TÍTULO / TITLE: - Penile cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Clark PE; Spiess PE; Agarwal N; Biagioli MC; Eisenberger MA; Greenberg RE; Herr HW; Inman BA; Kuban DA; Kuzel TM; Lele SM; Michalski J; Pagliaro L; Pal SK; Patterson A; Plimack ER; Pohar KS; Porter MP; Richie JP; Sexton WJ; Shipley WU; Small EJ; Trump DL; Wile G; Wilson TG; Dwyer M; Ho M

RESUMEN / SUMMARY: - Squamous cell carcinoma of the penis represents approximately 0.5% of all cancers among men in the United States and other developed countries. Although rare, it is associated with significant disfigurement, and only half of the patients survive beyond 5 years. Proper evaluation of both the primary lesion and lymph nodes is critical, because nodal involvement is the most important factor of survival. The NCCN Clinical Practice Guidelines in Oncology for Penile Cancer provide recommendations on the diagnosis and management of this devastating disease based on evidence and expert consensus.

TÍTULO / TITLE: - Renal angiomyolipoma with Fatty thrombus extending to the right atrium: an exceptional presentation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Nouira Y; Kallel Y; Gargouri M; Sellami A; Boulma R; Ziedi J; Chelif M; Ben Rhouma S; Kalfat T; Khayati A
INSTITUCIÓN / INSTITUTION: - Department of Urology, La Rabta University Hospital, 1007 Tunis, Tunisia.
RESUMEN / SUMMARY: - This paper reports the case of 34-year-old woman who presented with bilateral renal angiomyolipomas (AMLs). On the right side, there was a large AML with a fatty thrombus extending to the right atrium. The treatment consisted of right nephrectomy and complete thrombectomy with extracorporeal circulation and right atriotomy. Postoperatively, the patient was septic and died on postoperative day 7 because of septic shock.

TÍTULO / TITLE: - Primary testicular lymphoma with rupture: An unusual presentation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Vidyavathi K; Prabhakar K; Harendra KM
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Sri Devaraj Urs Medical College, Sri Devaraj Urs University, Tamaka, Kolar, Karnataka, India.

RESUMEN / SUMMARY: - Primary testicular lymphoma usually presents as a unilateral testicular mass with occasional bilateral involvement. The tumor show contiguous spread to rete testis, epididymis spermatic cord and rarely to tunica albuginea. We report a case of primary testicular lymphoma which showed rupture of tunica albuginea with involvement of inguinal lymph node which is unusual. A 50-year-old male patient presented with right inguinal swelling and right side scrotal swelling of five months’ duration. Fine needle aspiration of the right inguinal lymph node was done and was suggestive for lymphoma/seminoma. Histopathology of right orchiectomy revealed non-Hodgkin’s lymphoma (NHL). Further investigations did not reveal any other organs involved with non-Hodgkin’s lymphoma. Primary testicular lymphoma usually shows spread to extranodal sites like skin, central nervous system and Waldeyer’s ring at presentation and at relapse. Whereas, less common sites are lung, bone, liver, gastrointestinal system and nodal sites, especially the paraaortic lymph nodes. Testicular lymphoma with involvement of the inguinal lymph node is unusual. Clinical presentation of such cases may mimic germ cell tumors.

[1552]
TÍTULO / TITLE: - Management of locally advanced renal cell carcinoma with invasion of the duodenum.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: - Schlussel AT; Fowler AB; Chinn HK; Wong LL
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Tripler Army Medical Center, 1 Jarrett White Road, Honolulu, HI 96859, USA.

RESUMEN / SUMMARY: - Renal cell carcinoma (RCC) is rare but aggressive, with greater than 20% of patients presenting with stage III or IV, disease. Surgical resection of the primary tumor regardless of stage is the treatment of choice, and en bloc resection of involved organs provides the only potential chance for cure. This case report describes a patient with metastatic right-sided RCC with invasion of the inferior vena cava and duodenum managed by en block resection and pancreaticoduodenectomy. This report will review the workup and treatment of locally advanced RCC, as well as the role of cytoreductive nephrectomy in the setting of metastatic disease.

[1553]
Prostate cancer: Intermittent ADT—tales from a 27-year odyssey.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Klotz L
INSTITUCIÓN / INSTITUTION: University of Toronto, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, MG 408, Toronto, ON M4N 3M5, Canada. laurence.klotz@sunnybrook.ca.

Prostate cancer: A good night’s sleep might protect against prostate cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

Micropapillary urothelial carcinoma: Cytologic features in a retrospective series of urine specimens.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: Heymann JJ; Saqi A; Turk AT; Crapanzano J
INSTITUCIÓN / INSTITUTION: Department of Pathology and Cell Biology, New York-Presbyterian Hospital-Columbia University Medical Center, 630 West 168 Street, VC14-215, New York, NY 10032.

RESUMEN / SUMMARY: BACKGROUND: The micropapillary variant of urothelial carcinoma (uPC) is a rare variant of urothelial carcinoma that carries a poor prognosis. Definitive surgery may represent optimal management of low stage tumors. Urine cytology is indispensable in the screening and follow-up of urinary tract cancer. However, cytopathological criteria for diagnosis of uPC and its differentiation from conventional urothelial carcinoma (CUC) are not well-defined. MATERIALS AND METHODS: Twenty-five cases of histologically confirmed micropapillary uPC from 21 patients were compared to 25 cases of histologically confirmed high-grade CUC. RESULTS: In uPC cases, cell clusters were identified in 13 of 25 specimens from 10 patients. Six of the 13 specimens containing cell clusters corresponded to surgical pathology specimens in which micropapillary carcinoma accounted for at least 50% of total carcinoma. In contrast, only 1 of the 12 urine specimens devoid of cell clusters corresponded
to surgical specimens in which micropapillary carcinoma accounted for at least 50% of total carcinoma. Cytomorphologic features of urinary specimens from patients with histologically confirmed micropapillary carcinoma were generally similar to those from patients with high-grade CUC, making it difficult to distinguish these entities in exfoliative urine specimens. CONCLUSIONS AND SUMMARY: Further investigation of the core cytopathological characteristics of uPC is warranted to refine its diagnostic criteria by exfoliative urine cytology.

[1556]
TÍTULO / TITLE: - Metastatic urachal carcinoma in bronchial brush cytology.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Aly FZ; Tabbarah AZ; Voltaggio L
INSTITUCIÓN / INSTITUTION: - Department of Cytopathology, University of Arizona, Tucson, AZ.
RESUMEN / SUMMARY: - Urachal carcinoma is rare comprising less than 1% of all bladder carcinomas. Metastases of urachal carcinoma have been reported to meninges, brain, ovary, lung, and maxilla. Cytologic features of metastatic urachal carcinoma have not been previously reported. We present a case of metastatic urachal adenocarcinoma in bronchial brushings and review the use of immunohistochemistry in its diagnosis. A 47-year-old female was seen initially in 2007 with adenocarcinoma of the bladder dome for which she underwent partial cystectomy. She presented in 2011 with a left lung mass and mediastinal adenopathy. Bronchoscopy showed an endobronchial lesion from which brushings were obtained. These showed numerous groups of columnar cells with medium sized nuclei and abundant cytoplasm. The cells were positive for CK20 and CDX2 and negative for CK7. The cytomorphicological findings were similar to those in the previous resection specimen and concurrent biopsy. This is the first case report of bronchial brushings containing metastatic urachal carcinoma. No specific immunohistochemical profile is available for its diagnosis. The consideration of a second primary was a distinct possibility in this case due to the lapse of time from primary resection, absence of local disease, and lack of regional metastases.

[1557]
TÍTULO / TITLE: - Green tea polyphenols and cancer chemoprevention of genitourinary cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Green tea, which has higher concentrations of polyphenols than other teas, has been correlated with reduced risk of various malignancies with most data supporting a potential protective role in prostate neoplasia. Preclinical studies over the last 25 years implicate constituent green tea catechins, epigallocatechin-3-gallate (EGCG) being the predominant form, as the main mechanistic ingredient in the observed biologic effects, which vary from proapoptotic effects to inhibition of androgen receptor and signal transduction pathways. There have been few prospective clinical trials of green tea polyphenols (GTP), especially with well-characterized formulations and doses. Although there have been hints of beneficial clinical activity in prostate neoplasia, other studies have raised concerns about the limited bioavailability and very low target-tissue concentrations of GTPs. At present there is no proven role for GTP supplementation in the prevention of genitourinary (GU) malignancies, but novel GTP formulations and further clinical testing may still support a future for GTP supplementation in GU cancer prevention.

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Gynecologic bleeding revealing vaginal metastasis of renal cell carcinoma.

We report a case of a 75-year-old woman, who underwent radical right nephrectomy for a renal cell carcinoma. Tumour was classified pT3bN0M0 and grade I of Furhmann grading. One year later, scanner discovered mediastinal and lombo-aortic lymph nodes. She received 2 months of immunotherapy associated with bevacizumab, but stopped because of intolerance. She was readmitted in our institute for vaginal bleeding. Clinical investigations showed a vaginal mass and biopsy revealed a renal cell carcinoma metastasis. This case suggests that retrograde venous
dissemination may be at the origin of vaginal metastasis of renal cell carcinoma and emphasized the preventive value of early ligature of renal vein.

[1559]

**TÍTULO / TITLE:** Genistein up-regulates tumor suppressor microRNA-574-3p in prostate cancer.

**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** Chiyomaru T; Yamamura S; Fukuhara S; Hidaka H; Majid S; Saini S; Arora S; Deng G; Shahryari V; Chang I; Tanaka Y; Tabatabai ZL; Enokida H; Seki N; Nakagawa M; Dahiya R

**INSTITUCIÓN / INSTITUTION:** Department of Urology, San Francisco Veterans Affairs Medical Center and University of California San Francisco, San Francisco, California, USA.

**RESUMEN / SUMMARY:** Genistein has been shown to inhibit cancers both in vitro and in vivo, by altering the expression of several microRNAs (miRNAs). In this study, we focused on tumor suppressor miRNAs regulated by genistein and investigated their function in prostate cancer (PCa) and target pathways. Using miRNA microarray analysis and real-time RT-PCR we observed that miR-574-3p was significantly up-regulated in PCa cells treated with genistein compared with vehicle control. The expression of miR-574-3p was significantly lower in PCa cell lines and clinical PCa tissues compared with normal prostate cells (RWPE-1) and adjacent normal tissues. Low expression level of miR-574-3p was correlated with advanced tumor stage and higher Gleason score in PCa specimens. Re-expression of miR-574-3p in PCa cells significantly inhibited cell proliferation, migration and invasion in vitro and in vivo. miR-574-3p restoration induced apoptosis through reducing Bcl-xL and activating caspase-9 and caspase-3. Using GeneCodis software analysis, several pathways affected by miR-574-3p were identified, such as ‘Pathways in cancer’, ‘Jak-STAT signaling pathway’, and ‘Wnt signaling pathway’. Luciferase reporter assays demonstrated that miR-574-3p directly binds to the 3’ UTR of several target genes (such as RAC1, EGFR and EP300) that are components of ‘Pathways in cancer’. Quantitative real-time PCR and Western analysis showed that the mRNA and protein expression levels of the three target genes in PCa cells were markedly down-regulated with miR-574-3p. Loss-of-function studies demonstrated that the three target genes significantly affect cell proliferation, migration and invasion in PCa cell lines. Our results show that genistein up-regulates tumor suppressor miR-574-3p expression targeting several cell signaling pathways. These findings enhance understanding of how genistein regulates with miRNA in PCa.
[1560]
**TÍTULO / TITLE:** - What next for the small renal mass?
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
- Enlace al texto completo (gratuito o de pago) 1038/nrurol.2013.85
**AUTORES / AUTHORS:** - Payton S
**INSTITUCIÓN / INSTITUTION:** - Nature Reviews Urology.

[1561]
**TÍTULO / TITLE:** - BRCA1 and p53 regulate critical prostate cancer pathways.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
- Enlace al texto completo (gratuito o de pago) 1038/pcan.2013.12
**AUTORES / AUTHORS:** - De Luca P; Moiola CP; Zalazar F; Gardner K; Vazquez ES; De Siervi A
**INSTITUCIÓN / INSTITUTION:** - Department of Biological Chemistry, School of Sciences (FCEN), University of Buenos Aires (UBA), IQUIBICEN-CONICET, Buenos Aires, Argentina.
**RESUMEN / SUMMARY:** - Background: Loss or mutations of the BRCA1 gene are associated with increased risk of breast and ovarian cancers and with prostate cancer (PCa) aggressiveness. Previously, we identified GADD153 as a target of BRCA1 protein, which increases doxorubicin sensitivity in human p53-/- PCa cells (PC3). Considering that p53 is a crucial target in cancer therapy, in this work we investigated p53 role in the regulation of transcription of GADD153.
**Methods:** We performed reverse transcription quantitative PCR (RT-qPCR), western blot and luciferase assays to analyze GADD153 and/or BRCA1 expression in response to ultraviolet or doxorubicin exposure in PC3 p53 stable-transfected cells and LNCaP (p53+/+) cells. BRCA1 protein recruitment to GADD153 promoter was studied by chromatin immunoprecipitation-qPCR. To assess expression of BRCA1 and/or p53 target genes, we used a panel of stable-transfected PCa cell lines. We finally analyzed these genes in vivo using BRCA1-depleted PCa xenograft models.
**Results:** We found that GADD153 was highly induced by doxorubicin in PC3 cells; however, this response was totally abolished in LNCaP (p53wt) and in p53-restituted PC3 cells. Furthermore, BRCA1 protein associates to GADD153 promoter after DNA damage in the presence of p53. Additionally, we demonstrated that BRCA1 and/or p53 modulate genes involved in DNA damage and cell cycle regulation (cyclin D1, BLM, BRCA2, DDB2, p21WAF1/CIP1, H3F3B, GADD153, GADD45A, FEN1, CCNB2), EMT (E-cadherin, beta-catenin, vimentin, fibronectin, slug, snail) and Hedgehog pathways (SHH, IHH, DHH, Gli1, PATCH1). Furthermore, xenograft
studies demonstrated that BRCA1 knockdown in PC3 cells increased tumor growth and modulated these genes in vivo. Conclusions: Although BRCA1 induces GADD153 in a p53 independent manner, p53 abolished GADD153 induction in response to DNA damage. In addition, several important PCa targets are modulated by BRCA1 and p53. Altogether, these data might be important to understand the therapy response of PCa patients. Prostate Cancer and Prostatic Disease advance online publication, 14 May 2013; doi:10.1038/pcan.2013.12.

[1562] TÍTULO / TITLE: - The role of naftopidil in the management of benign prostatic hyperplasia.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
●● Enlace al texto completo (gratuito o de pago)
1177_1756287212461681 [pii]
●● Enlace al texto completo (gratuito o de pago)
1177/1756287212461681 [pii]
AUTORES / AUTHORS: - Hara N; Mizusawa T; Obara K; Takahashi K
INSTITUCIÓN / INSTITUTION: - Division of Urology, Department of Regenerative and Transplant Medicine, Graduate School of Medical and Dental Sciences, Niigata University, Asahimachi 1, Niigata 951-8510, Japan.
RESUMEN / SUMMARY: - Naftopidil, which to a certain extent shows an affinity to alpha1D-adrenoceptor subtype in addition to a high affinity to alpha1A-adrenoceptor, has been used for the treatment of benign prostatic obstruction and benign prostatic hyperplasia (BPH) associated lower urinary tract symptoms (LUTS). The aim of the present review is to systematically refer to the published studies on this unique agent for BPH. Based on a randomized prazosin-controlled study and another double-blind placebo-controlled study, which verified the dose-dependent effects of naftopidil, the Japanese Ministry of Health, Labor and Welfare approved naftopidil for treating men with BPH in 1996. Several tamsulosin-controlled studies have suggested treatment effects of naftopidil similar to those of tamsulosin and potentially higher efficacy for alleviating storage symptoms by naftopidil. Although well-designed, randomized studies are warranted to confirm the long-term outcomes and effector/target of naftopidil, the alpha1A-antagonist naftopidil, which also blocks alpha1D-adrenoceptor, improves voiding symptoms, and may also be useful for the management of men with storage symptoms represented by nocturia, retrieving their quality of life impaired by BPH-associated LUTS.

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[1563]
**Título / Title:** Multiple joint metastasis of a transitional cell carcinoma in a dog.

**Resumen / Summary:** An 8-year-old castrated male hound mix was referred to the Purdue University Veterinary Teaching Hospital for severe lameness, pollakiuria, and dyschezia. On presentation, the dog was non-weight bearing on the right rear limb and the right carpus was diffusely swollen. Synovial fluid analysis from the right carpus revealed a population of epithelial cells displaying marked anisocytosis, anisokaryosis, multinucleation, and prominent, variably sized nucleoli. A metastatic carcinoma with presumed prostatic or urothelial origin was diagnosed based on cytomorphology. Subsequent cytologic evaluation of peripheral lymph nodes revealed the presence of a similar neoplastic population. The dog was euthanized and synovial fluid from both stifle joints, as well as impression smears of the prostate gland, were collected. Carcinoma cells were identified in each stifle joint and in the prostate gland. Immunocytochemistry was performed on synovial fluid smears from 2 of the joints (right stifle and right carpus) and on impression smears of the prostate gland. The neoplastic population in the joints and prostate gland showed strong immunoreactivity to uroplakin III, a urothelial marker, indicating metastasis of a transitional cell carcinoma to multiple joints. In addition, evidence for epithelial to mesenchymal transition was identified using cytokeratin, an epithelial marker, and vimentin, a mesenchymal marker. A necropsy was performed and histopathology confirmed the presence of metastatic transitional cell carcinoma in various tissues. This case illustrates the importance of considering metastatic disease when a patient is presented with severe lameness and joint pain, and the clinical utility of synovial fluid cytology for diagnosis of metastasis in these cases.


**Autores / Authors:** Colledge SL; Raskin RE; Messick JB; Tiffany Reed L; Wigle WL; Balog KA

**Institución / Institution:** Department of Comparative Pathobiology, Purdue University College of Veterinary Medicine, West Lafayette, IN, USA.
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Shizuoka City Shimizu Hospital Shimizu, Shizuoka, Japan.

[1565]

TÍTULO / TITLE: - ARID1A Alterations Are Associated with FGFR3-Wild Type, Poor-Prognosis, Urothelial Bladder Tumors.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

AUTORES / AUTHORS: - Balbas-Martinez C; Rodriguez-Pinilla M; Casanova A; Dominguez O; Pisano DG; Gomez G; Lloreta J; Lorente JA; Malats N; Real FX
INSTITUCIÓN / INSTITUTION: - Epithelial Carcinogenesis Group, Molecular Pathology Programme, Spanish National Cancer Research Centre, Madrid, España.
RESUMEN / SUMMARY: - Urothelial bladder cancer (UBC) is heterogeneous at the clinical, pathological, genetic, and epigenetic levels. Exome sequencing has identified ARID1A as a novel tumor suppressor gene coding for a chromatin remodeling protein that is mutated in UBC. Here, we assess ARID1A alterations in two series of patients with UBC. In the first tumor series, we analyze exons 2-20 in 52 primary UBC and find that all mutant tumors belong to the aggressive UBC phenotype (high grade non-muscle invasive and muscle invasive tumors) (P = 0.05). In a second series (n = 84), we assess ARID1A expression using immunohistochemistry, a surrogate for mutation analysis, and find that loss of expression increases with higher stage/grade, it is inversely associated with FGFR3 overexpression (P = 0.03) but it is not correlated with p53 overexpression (P = 0.30). We also analyzed the expression of cytokeratins in the same set of tumors and find, using unsupervised clustering, that tumors with ARID1A loss of expression are generally KRT5/6-low. In this patient series, loss of ARID1A expression is also associated with worse prognosis, likely reflecting the higher prevalence of losses found in tumors of higher stage and grade. The independent findings in these two sets of patients strongly support the notion that ARID1A inactivation is a key player in bladder carcinogenesis occurring predominantly in FGFR3 wild type tumors.

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[1566]

TÍTULO / TITLE: - Quality indicators in the management of bladder cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Montgomery JS; Miller DC; Weizer AZ
INSTITUCIÓN / INSTITUTION: - Department of Urology, University of Michigan, Ann Arbor, Michigan, USA. montrose@umich.edu
RESUMEN / SUMMARY: - Bladder cancer is predominantly seen in elderly patients. With the aging United States population, the incidence and prevalence of bladder cancer are on the rise, heightening the relevance of this disease as a public health issue. Despite having one of the greatest average cancer treatment costs per patient, improvements in disease-specific survival have been subtle. Clinical guidelines based predominantly on expert opinion and randomized controlled studies offer some guidance, but adherence to these guidelines is lacking. Building awareness of quality indicators to optimize patient care represents an opportunity to improve bladder cancer outcomes. Although quality indicators exist for other disease states, widely accepted quality indicators for the management of bladder cancer have not yet been established. This article proposes an initial set of quality indicators for both non-muscle-invasive and muscle-invasive bladder cancer based on established clinical guidelines and the available literature.

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[1567]
TÍTULO / TITLE: - Simvastatin Inhibits Renal Cancer Cell Growth and Metastasis via AKT/mTOR, ERK and JAK2/STAT3 Pathway.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Fang Z; Tang Y; Fang J; Zhou Z; Xing Z; Guo Z; Guo X; Wang W; Jiao W; Xu Z; Liu Z
INSTITUCIÓN / INSTITUTION: - Department of Urology, Qilu Hospital of Shandong University, Ji‘nan, Shandong, China ; The Key Laboratory of Cardiovascular Remodeling and Function Research, Chinese Ministry of Education and Chinese Ministry of Public Health, Qilu Hospital of Shandong University, Ji‘nan, Shandong, China.
RESUMEN / SUMMARY: - Renal cell carcinoma (RCC) is the most lethal type of genitourinary cancer due to its occult onset and resistance to chemotherapy and radiation. Recently, accumulating evidence has suggested stains, inhibitors of 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase, were associated with the risk reduction of cancer. In the present study, we aimed to investigate the potential effects of simvastatin on RCC cells and the underlying mechanisms by which simvastatin exerted its actions. With cell viability, colony formation, and flow cytometric apoptosis assays, we found that simvastatin potently suppressed cell growth of A498 and 786-O cells in a time- and dose-dependent manner. Consistently, the xenograft model performed in nude mice exhibited reduced tumor growth with simvastatin treatment. In addition, the inhibitory effects of simvastatin on migration and invasion were also observed in vitro. Mechanically, we presented that simvastatin could suppress the
proliferation and motility of RCC cells via inhibiting the phosphorylation of AKT, mTOR, and ERK in a time- and dose-dependent manner. Further investigation of the underlying mechanism revealed simvastatin could exert the anti-tumor effects by suppressing IL-6-induced phosphorylation of JAK2 and STAT3. In conclusion, these findings suggested that simvastatin-induced apoptosis and its anti-metastasis activity in RCC cells were accompanied by inhibition of AKT/mTOR, ERK, and JAK2/STAT3 pathways, which imply that simvastatin may be a potential therapeutic agent for the treatment of RCC patients.

[1568]
TITULO / TITLE: - Bladder cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Clark PE; Agarwal N; Biagioli MC; Eisenberger MA; Greenberg RE; Herr HW; Inman BA; Kuban DA; Kuzel TM; Lele SM; Michalski J; Pagliaro LC; Pal SK; Patterson A; Plimack ER; Pohar KS; Porter MP; Richie JP; Sexton WJ; Shipley WU; Small EJ; Spiess PE; Trump DL; Wile G; Wilson TG; Dwyer M; Ho M
INSTITUCIÓN / INSTITUTION: - Vanderbilt-Ingram Cancer Center.
RESUMEN / SUMMARY: - Bladder cancer is the fourth most common cancer in the United States. Urothelial carcinoma that originates from the urinary bladder is the most common subtype. These NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) provide recommendations on the diagnosis and management of non-muscle-invasive and muscle-invasive urothelial carcinoma of the bladder. This version of the guidelines provides extensive reorganization and updates on the principles of chemotherapy management.

[1569]
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Kapoor S
INSTITUCIÓN / INSTITUTION: - Mechanicsville, VA.

[1570]
TITULO / TITLE: - Prostate adenocarcinoma with a rectal metastasis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

Enlace a la Editora de la Revista http://bmj.com/search.dtl
Lo que puede esconder una meralgia parestesica: tumor renal como causa infrecuente.

Meralgia paresthetica is a mononeuropathy of the femoral cutaneous nerve with characteristic findings, usually secondary to injury or compression, being most common in the inguinal area. Exceptional cases associated with compressions caused by abdominal or pelvic tumors have been published, so it is always advisable to extend the study with imaging tests. We present a case associated with a renal tumor.

Overexpression of EZH2 and other PRC2 subunits, such as SUZ12, is associated with tumor progression and poor prognosis in several human malignancies. Nevertheless, the underlying mechanisms driving aberrant EZH2 expression are poorly understood. This review provides...
molecular insights into the essential role of EZH2 in breast and prostate tumorigenesis. We addressed the current understanding on the oncogenic role of EZH2, with an emphasis on: (1) the less known PRC2-independent role of EZH2 in gene activation, in addition to its canonical role in transcriptional silencing as a histone methyltransferase catalyzing the trimethylation of histone H3 at lysine 27; (2) causes and consequences of its deregulation in tumor cells and; (3) collaboration of EZH2 with other epigenetic and hormone receptor-mediated oncogenic signaling pathways. We also summarize how EZH2 has emerged as a promising therapeutic target in hormone-refractory cancers and the prospects for integrating EZH2 blockade with available pharmacological inhibitors.

[1573]
TÍTULO / TITLE: - Effects of di(n-butyl) and monobutyl phthalate on steroidogenesis pathways in the murine Leydig tumor cell line MLTC-1.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Chen X; Zhou QH; Leng L; Chen X; Sun ZR; Tang NJ
INSTITUCIÓN / INSTITUTION: - Department of Occupational and Environmental Health, School of Public Health, Tianjin Medical University, Qixiangtai Road No. 22, Heping District, Tianjin 300070, China.
RESUMEN / SUMMARY: - Di(n-butyl) phthalate (DBP) and its active metabolite monobutyl phthalate (MBP) have been shown to disrupt reproductive organ growth. The objective of this study was to evaluate the effects of DBP/MBP on steroidogenesis in the murine Leydig tumor cell line MLTC-1 in vitro. MLTC-1 cells were incubated with various concentrations of DBP (100, 1, 0.01, and 0mumol/l in DMSO) and MBP (1000, 10, 0.1, and 0mumol/l in DMSO) for 24h. Testosterone secretion was stimulated at the lowest doses and inhibited at higher treatment doses of DBP and MBP. The mRNA levels of the side-chain cleavage enzyme (P450scc), cytochrome p450c17 (P450c17) and 3beta-hydroxy-steroid dehydrogenase (3betaHSD) were significantly reduced in the phthalate-exposed groups, whereas, the transcription and translation of insulin-like hormone 3 (INSL3) was affected by DBP and MBP. Alterations of the steroidogenic enzymes and INSL3 in MLTC-1 cells may be involved in the biphasic effects of DBP/MBP on androgen production.

[1574]
TÍTULO / TITLE: - Application of the Modified Clavien Classification System to 120W Greenlight High-Performance System Photoselective Vaporization of the Prostate for Benign Prostatic Hyperplasia: Is It Useful for Less-Invasive Procedures?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace al texto completo (gratuito o de pago) 4111/kju.2013.54.4.239
AUTORES / AUTHORS: - Kwon O; Park S; Jeong MY; Cho SY; Son H
INSTITUCIÓN / INSTITUTION: - Department of Urology, SMG-SNU Boramae Medical Center, Seoul, Korea.
RESUMEN / SUMMARY: - PURPOSE: To evaluate the accuracy and applicability of the modified Clavien classification system (CCS) in evaluating complications following photoselective vaporization of the prostate by use of the 120W GreenLight high-performance system (HPS-PVP). MATERIALS AND METHODS: The medical records of 342 men who underwent HPS-PVP were retrospectively analyzed. Patients were older than 40 years and had a prostate volume >30 mL and an International Prostate Symptom Score (IPSS) >/=8. Patients with prostatic malignancy, neurogenic bladder, urethral stricture, large postvoid residual volume (>250 mL), previous prostatic surgery, or urinary tract infection were excluded. All operations were done by a single surgeon, and patients were followed up for uroflowmetry and IPSS postoperatively. All complications were recorded and classified according to the modified CCS, and methods of management were also recorded. RESULTS: The patients’ mean age was 71.6+/-7.3 years; mean prostate volume was 50.0+/-17.0 mL, and 95 cases (27.7%) had volumes greater than 70 mL. The mean total IPSS was 21.7+/-7.9 preoperatively and 12.3+/-8.1 at the first month postoperatively. A total of 59 patients (17.3%) experienced postoperative complications until the first month after the surgery. Among them, 49 patients (14.3%) showed grade I complications, 9 patients (2.6%) showed grade II complications, and 1 patient (0.3%) showed a grade IIIb complication. No patients had complications graded higher than IIIb. CONCLUSIONS: Although the modified CCS is a useful tool for communication among clinicians in allowing comparison of surgical outcomes, this classification should be revised to gain higher accuracy and applicability in the evaluation of postoperative complications of HPS-PVP.
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[1575]
TÍTULO / TITLE: - Acute cord compression secondary to spinal relapse of testicular seminomas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
   ●●Enlace a la Editora de la Revista http://bmj.com/search.dtl
   ●●Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-008863
AUTORES / AUTHORS: - Ng YH; Ho HS; Kumar NS
This is the first-reported case of an isolated thoracic spine relapse of a stage 1 testicular seminoma more than 1 year after surgery and radiotherapy. We report a 38-year-old gentleman, who underwent radical orchidectomy and adjuvant retroperitoneal irradiation for a pure testicular seminoma, presenting with acute cord compression from an isolated T8 relapse 14 months after the index surgery. Decompressive laminectomy with instrumentation was performed with adjuvant chemoradiotherapy. The patient gained full neurological recovery and has remained disease-free for 4 years. Testicular seminomas rarely relapse in the spine after treatment with surgery and radiotherapy, and it is usually the lumbar spine that is involved. Spinal relapse also commonly presents with pain rather than acute cord compression. This case report discusses the unique behaviour of testicular seminomas and their presentation in vertebral relapse. We also present a summary of the available literature on isolated thoracic spine relapse of testicular seminomas.

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[1576]

TÍTULO / TITLE: Potential value of Gleason score in predicting the benefit of cabazitaxel in metastatic castration-resistant prostate cancer.
RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: Buonerba C; Pond GR; Sonpavde G; Federico P; Rescigno P; Puglia L; Bosso D; Virtuoso A; Policastro T; Izzo M; Vaccaro L; Ferro M; Aieta M; Perdona S; Palmieri G; De Placido S; Di Lorenzo G

INSTITUCIÓN / INSTITUTION: Genitourinary Cancer Section, Medical Oncology Division, Department of Endocrinology & Oncology, University Federico II, Napoli, Italy.
RESUMEN / SUMMARY: Aim: This study aimed to identify predictive/prognostic factors in castration-resistant prostate cancer patients treated with cabazitaxel. Patients & methods: Patients were enrolled from March 2011 to December 2011 in an international expanded access program. In January 2012, when cabazitaxel became commercially available, a prospective study was initiated at University Federico II of Naples and at Rionero in Vulture Hospital. Results: Forty-seven patients were enrolled in this study. Patients received a median of nine cycles of cabazitaxel. Median progression-free survival was 7.0 months (95% CI: 5.7-8.0). Seventeen patients were still alive at the time of the analysis, with a median overall survival of 14 months (95% CI: 11-16). At multivariate analysis, a higher Gleason score (>/=8) appeared to be associated with prolonged progression-free survival (hazard ratio: 0.36; 95% CI: 0.18-0.72); however, the higher Gleason score showed no statistical impact on overall
survival. Conclusion: We hypothesize that the Gleason score has the potential to be incorporated in the clinical decision-making process for definition of treatment strategy in docetaxel-pretreated castration-resistant prostate cancer patients. We encourage further experimentation in this setting.

[1577]

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Abrich V; Duvuru S; Swanson HJ
INSTITUCIÓN / INSTITUTION: - *Department of Internal Medicine, Marshfield Clinic; Marshfield, Wisconsin.
RESUMEN / SUMMARY: - Connective tissue disorders increase the risk of malignancy; conversely, they may manifest as rheumatological paraneoplastic syndromes due to an underlying malignancy. We describe a patient with limited scleroderma whose rapid disease progression coincided with the discovery of a renal tumor. A female patient, aged 75 years, presented with a 3-month history of progressive difficulty grasping objects, unsteadiness, dyspnea, xerostomia, xerophthalmia, and significant weight loss. She had a 10-year history of gastroesophageal reflux and Raynaud’s phenomenon. Pertinent physical examination findings included facial telangiectasias, bibasilar inspiratory rales, sclerodactyly, and absent pinprick and vibratory sensation in her toes. She also had swelling and tenderness in several metacarpophalangeal and interphalangeal joints and both ankles. A renal mass was demonstrated on abdominal computed tomography. A left partial nephrectomy was performed, confirming an unclassified type of renal cell carcinoma, along with a focal proliferative crescentic pauci-immune glomerulonephritis. Medical therapy with rituximab, pulse methylprednisolone, and prednisone led to improvement in her symptoms. The patient’s presentation is consistent with a rapid progression of pre-existing limited scleroderma with the development of new rheumatological symptoms, including vasculitis. We propose that this progression was secondary to paraneoplastic stimulation by the renal cell carcinoma. Clinicians should consider looking for a malignancy in patients with connective tissue disorders who present with a myriad of new symptoms.

[1578]

TÍTULO / TITLE: - Anti-CD70 Immunocytokines for Exploitation of Interferon-gamma-Induced RIP1-Dependent Necrosis in Renal Cell Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
Metastatic renal cell carcinoma (RCC) is an incurable disease in clear need of new therapeutic interventions. In early-phase clinical trials, the cytokine IFN-gamma showed promise as a biotherapeutic for advanced RCC, but subsequent trials were less promising. These trials, however, focused on the indirect immunomodulatory properties of IFN-gamma, and its direct anti-tumor effects, including its ability to kill tumor cells, remains mostly unexploited. We have previously shown that IFN-gamma induces RIP1 kinase-dependent necrosis in cells lacking NF-kappaB survival signaling. RCC cells display basally-elevated NF-kappaB activity, and inhibiting NF-kappaB in these cells, for example by using the small-molecule proteasome blocker bortezomib, sensitizes them to RIP1-dependent necrotic death following exposure to IFN-gamma. While these observations suggest that IFN-gamma-mediated direct tumoricidal activity will have therapeutic benefit in RCC, they cannot be effectively exploited unless IFN-gamma is targeted to tumor cells in vivo. Here, we describe the generation and characterization of two novel ‘immunocytokine’ chimeric proteins, in which either human or murine IFN-gamma is fused to an antibody targeting the putative metastatic RCC biomarker CD70. These immunocytokines display high levels of species-specific IFN-gamma activity and selective binding to CD70 on human RCC cells. Importantly, the IFN-gamma immunocytokines function as well as native IFN-gamma in inducing RIP1-dependent necrosis in RCC cells, when deployed in the presence of bortezomib. These results provide a foundation for the in vivo exploitation of IFN-gamma-driven tumoricidal activity in RCC.

[1579]

**TÍTULO / TITLE:**  - An introduction to acinar pressures in BPH and prostate cancer.

**RESUMEN / SUMMARY:**  - [Enlace al Resumen / Link to its Summary](http://1038/nrurol.2013.86)


**AUTORES / AUTHORS:**  - Wadhera P

**INSTITUCIÓN / INSTITUTION:**  - The Brooklyn Hospital Center, Department of Surgery, 240 Willoughby Street, Brooklyn, NY 11201, USA. paw9070@nyp.org.

**RESUMEN / SUMMARY:**  - Intra-acinar and peri-acinar pressures in the prostate might be key factors in the evolution of its zonal morphology and the pathogenesis of BPH and cancer. Herein, I hypothesize that intra-acinar
pressures lead to a decrease in apoptosis by distending or stretching acinar epithelium and its surrounding stroma. Increased prostatic smooth muscle content and tone might generate peri-acinar pressures, which could, in the long-term, counteract intra-acinar pressures and decrease epithelial stretch. Thus, it is proposed that BPH (characterized by increased prostatic smooth muscle and, therefore, raised peri-acinar pressures) might decrease the risk of prostate cancer progression by counteracting intra-acinar pressures. In the context of this theory, the transition zone might have evolved as a specialized region within the prostate that can mount a concerted stromal-epithelial response to increased urethral and intra-acinar pressures (BPH), and the urethral angulation, anterior stroma and the prostatic capsule have an adjunctive evolutionary role in this phenomenon.

[1580]

TÍTULO / TITLE: - Mixed collecting duct and renal cell carcinoma presenting with spinal cord compression.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

●●Enlace a la Editora de la Revista http://bmj.com/search.dtl
●●Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-008987

AUTORES / AUTHORS: - Hennessey DB; Thomas AZ; Lynch TH
INSTITUCIÓN / INSTITUTION: - Department of Urology, Craigavon Area Hospital, Portadown, Northern Ireland, UK. derek.hennessey@gmail.com

RESUMEN / SUMMARY: - Collecting duct carcinoma (CDC) is a rare renal malignancy thought to develop from the collecting duct epithelium of the kidney. CDC tends to have a more aggressive clinical course than conventional renal cell carcinoma (RCC), with early metastases. The occurrence of a mixed CDC and conventional RCC is infrequently reported in the literature. We report the first case of a metastatic mixed CDC and RCC presenting as back pain in a young adult. In addition we discuss the epidemiology of and current adjuvant therapies for CDC.

[1581]

TÍTULO / TITLE: - Perlman syndrome: overgrowth, Wilms tumor predisposition and DIS3L2.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

●●Enlace al texto completo (gratuito o de pago) 1002/ajmg.c.31358

AUTORES / AUTHORS: - Morris MR; Astuti D; Maher ER

1123
Perlman syndrome is a rare autosomal recessively inherited congenital overgrowth syndrome characterized by polyhydramnios, macrosomia, characteristic facial dysmorphology, renal dysplasia and nephroblastomatosis and multiple congenital anomalies. Perlman syndrome is associated with high neonatal mortality and, survivors have developmental delay and a high risk of Wilms tumor. Recently a Perlman syndrome locus was mapped to chromosome 2q37 and homozygous or compound heterozygous mutations were characterized in DIS3L2. The DIS3L2 gene product has ribonuclease activity and homology to the DIS3 component of the RNA exosome. It has been postulated that the clinical features of Perlman syndrome result from disordered RNA metabolism and, though the precise targets of DIS3L2 have yet to be characterized, in cellular models DIS3L2 knockdown is associated with abnormalities of cell growth and division.

[1582]

Primary large cell neuroendocrine carcinoma of the ureter.

Large cell neuroendocrine carcinoma (LCNEC) is the rarest type of urinary tract malignancy. Herein, we report a case of LCNEC that arose in the ureter of a 78-year-old Japanese man with a history of ascending colon cancer that had been excised by a right hemicolectomy. Left-sided hydronephrosis associated with the ureteral tumor was discovered during follow-up. A left nephroureterectomy combined with a partial resection of the urinary bladder was performed because atypical cells were detected using voided urine cytology. A histopathological examination revealed that the ureteral tumor contained large atypical epithelial cells of neuroendocrine morphology without a urothelial carcinomatous component. The neoplastic cells were immunohistochemically positive for synaptophysin, chromogranin A, CD56, and cytokeratins, but they were negative for uroplakin III and thyroid transcription factor-1. The Ki-67 labeling index of the neoplastic cells was 50%. Transmission electron microscopy demonstrated the presence of numerous dense granules in the cytoplasm of the neoplastic cells. The ureteral lesion was finally classified as stage III, pT3 cN0 cM0. The patient’s postoperative course was uneventful without chemoradiotherapy, and LCNEC did not recur in the subsequent nine months. This case demonstrates that LCNEC can occur in the ureter, which normally does not contain neuroendocrine cells in the urothelium.
Correction to inherently multimodal nanoparticle-driven tracking and real-time delineation of orthotopic prostate tumors and micrometastases.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Liu TW; Macdonald TD; Jin CS; Gold JM; Bristow RG; Wilson BC; Zheng G

Dual inhibition of autophagy and the AKT pathway in prostate cancer.

RESUMEN / SUMMARY: Enlace al Resumen / Link to its Summary


AUTORES / AUTHORS: Lamoureux F; Zoubeidi A

INSTITUCIÓN / INSTITUTION: The Vancouver Prostate Centre; Department of Urologic Sciences; University of British Columbia; Vancouver, BC Canada.

RESUMEN / SUMMARY: Genetic inactivation of PTEN through either gene deletion or mutation is common in metastatic prostate cancer, leading to activation of the phosphoinositide 3-kinase (PI3K-AKT) pathway, which is associated with poor clinical outcomes. The PI3K-AKT pathway plays a central role in various cellular processes supporting cell growth and survival of tumor cells. To date, therapeutic approaches to develop inhibitors targeting the PI3K-AKT pathway have failed in both pre-clinical and clinical trials. We showed that a novel AKT inhibitor, AZD5363, inhibits the AKT downstream pathway by reducing p-MTOR and p-RPS6KB/p70S6K. We specifically reported that AZD5363 monotherapy induces G2 growth arrest and autophagy, but fails to induce significant apoptosis in PC-3 and DU145 prostate cancer cell lines. Blocking autophagy using pharmacological inhibitors (3-methyladenine, chloroquine and bafilomycin A 1) or genetic inhibitors (siRNA targeting ATG3 and ATG7) enhances cell death induced by AZD5363 in these prostate cancer cells. Importantly, the combination of AZD5363 with chloroquine significantly reduces tumor volume compared with the control group, and compared with either drug alone in prostate tumor xenograft models. Taken together, these data demonstrate that AKT inhibitor AZD5363, synergizes with the lysosomotropic inhibitor of autophagy, chloroquine, to induce apoptosis and delay tumor progression in prostate cancer models that are resistant to monotherapy, with AZD5363 providing a new therapeutic approach potentially translatable to patients.
Impact of lymphadenectomy in management of renal cell carcinoma.

PURPOSE: To evaluate the impact of regional lymphadenectomy as part of a management plan on morbidity, mortality and survival in renal cell carcinoma (RCC). PATIENTS AND METHODS: A retrospective study reviewing 158 cases diagnosed as RCC at the National Cancer Institute, Cairo University, Egypt, during the time period from 2000 to 2007. Histopathological data and significant operative and postoperative events were retrieved to compare three lymphadenectomy groups; Group A, where more than 5 nodes were dissected, Group B where 5 or less nodes were dissected and Group C where no nodal dissection was done. RESULTS: More positive lymph nodes were seen in group A (37.8%) compared to group B (9.6%) (p=0.002). Lymph node positivity was significantly associated with higher grade (p=0.005), but not with larger tumor size (p=0.221). There was no significant difference in overall survival between the three lymphadenectomy groups (p=0.163). Overall survival was not significantly affected by lymph node status (p=0.585). CONCLUSION: Regional lymphadenectomy in RCC has no impact on the mortality or morbidity.

Surveillance for urinary tract cancer in Lynch syndrome.

Hereditary non-polyposis colorectal cancer (HNPCC) is an inherited multiorgan cancer syndrome, which when caused by a germline mutation in the mismatch repair (MMR) genes is known as Lynch syndrome (LS). Mutation carriers are at risk for developing cancers primarily in the colon, rectum and endometrium, but also other extra-colonic cancers. Urinary tract cancers (UTC) have in many studies been reported increased in LS and it has...
been discussed among researchers and clinicians whether or not screening for urological tumours should be included in the surveillance programme and if so what screening procedures are justifiable. The aim of this review was to elucidate the present knowledge from the literature on the risk of UTC in LS and highlight the pros and cons of screening for asymptomatic neoplasia in the urinary tract. The review is based on a systematic literature search in PubMed database followed by a reference list of retrieved articles and manual searches of further relevant articles. In conclusion there is a moderate increased risk of UTC in LS, but a tremendous lack of knowledge on which screening programme, if any at all to establish, and if so what procedures and time intervals are appropriate. It is recommended that all eventually screening for UTC in LS, only should be performed in clinical trials or with a systematic reporting to a HNPCC-register for future evaluation.

[1587]

**TITULO / TITLE:** - Androgen deprivation for prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratis o de pago)

1200/EdBook_AM.2013.33.e176

**AUTORES / AUTHORS:** - Chi KN; Nguyen PL; Higano CS

**INSTITUCIÓN / INSTITUTION:** - From the BC Cancer Agency - Vancouver Cancer Centre, Vancouver, British Columbia, Canada; Dana-Farber Cancer Institute, Boston, MA; University of Washington, Fred Hutchinson Cancer Research Center, Seattle, WA.

**RESUMEN / SUMMARY:** - Androgen deprivation therapy (ADT) is the mainstay systemic treatment of prostate cancer because of the androgen dependence of the disease. Although ADT has long been used to manage prostate cancer, its use continues to evolve as data from clinical trials mature and long-term effects are recognized. For patients with localized disease and high-risk features, short and long courses of ADT as neoadjuvant/adjuvant therapy have been shown to improve survival when used with radiation therapy, but this has not been demonstrated with radical prostatectomy. The role of ADT with salvage radiotherapy after radical prostatectomy continues to be defined. Lifelong ADT in patients with node-positive disease after surgery or with radiation is also associated with increased survival. Increasingly though, the adverse effects of ADT that go beyond those on libido and hot flashes are being acknowledged. The metabolic effects on lipids, glycemic control, and bone loss from ADT can lead to an increased risk of cardiovascular events and osteoporosis, which needs to be considered when deciding to initiate and treat patients with ADT. Large, randomized trials comparing intermittent to continuous ADT have now been reported. Although the hope for improved cancer outcomes with
interrupted approach to therapy may help mitigate some of the negative effects of ADT in selected patients by allowing for off-treatment intervals.

[1588]
**TITULO / TITLE:** - Metastatic squamous cell carcinoma of the kidney from cholangiocarcinoma.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Choi H; Noh TI; Ham BK; Park JY; Shim KS; Bae JH

**INSTITUCIÓN / INSTITUTION:** - Department of Urology, Korea University Ansan Hospital, Korea University College of Medicine, Ansan, Korea.

**RESUMEN / SUMMARY:** - We present a rare case of a metastatic renal tumor originating from adenosquamous carcinoma of the intrahepatic bile duct. A 64-year-old man treated with bisegmentectomy and extended cholecystectomy for cholangiocarcinoma had a left cystic renal mass, which had irregular wall thickening, heterogeneously low attenuation, and soft tissue infiltration as determined by a computed tomography scan. The first impression was renal abscess. Left nephrectomy was performed and the nonencapsulated mass was gray in color macroscopically. Histological examination of the specimen revealed alveolar proliferation of small cancer cells, which was consistent with the original tumor of the intrahepatic bile duct. The left renal tumor was misdiagnosed as a renal abscess but finally diagnosed as squamous cell carcinoma metastasized from the intrahepatic bile duct. The patient expired because of lung metastasis after 14 months following left nephrectomy. In our opinion, this case would be the first report of a renal metastasis from a cholangiocarcinoma clinically and was treated with nephrectomy.

[1589]
**TITULO / TITLE:** - The genomic landscape of prostate cancer.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


**AUTORES / AUTHORS:** - Spans L; Clinckemalie L; Helsen C; Vanderschueren D; Boonen S; Lerut E; Joniau S; Claessens F

**INSTITUCIÓN / INSTITUTION:** - Molecular Endocrinology Laboratory, Department of Cellular and Molecular Medicine, University of Leuven, Campus Gasthuisberg, Herestraat 49, P.O. Box 901, 3000 Leuven, Belgium. frank.claessens@med.kuleuven.be.
**RESUMEN / SUMMARY:** - By the age of 80, approximately 80% of men will manifest some cancerous cells within their prostate, indicating that prostate cancer constitutes a major health burden. While this disease is clinically insignificant in most men, it can become lethal in others. The most challenging task for clinicians is developing a patient-tailored treatment in the knowledge that this disease is highly heterogeneous and that relatively little adequate prognostic tools are available to distinguish aggressive from indolent disease. Next-generation sequencing allows a description of the cancer at an unprecedented level of detail and at different levels, going from whole genome or exome sequencing to transcriptome analysis and methylation-specific immunoprecipitation, followed by sequencing. Integration of all these data is leading to a better understanding of the initiation, progression and metastatic processes of prostate cancer. Ultimately, these insights will result in a better and more personalized treatment of patients suffering from prostate cancer. The present review summarizes current knowledge on copy number changes, gene fusions, single nucleotide mutations and polymorphisms, methylation, microRNAs and long non-coding RNAs obtained from high-throughput studies.

[1590]

**TÍTULO / TITLE:** - D-pinitol Inhibits Prostate Cancer Metastasis through Inhibition of alphaVbeta3 Integrin by Modulating FAK, c-Src and NF-kappaB Pathways.

**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary


●●Enlace al texto completo (gratuito o de pago) 3390/ijms14059790

**AUTORES / AUTHORS:** - Lin TH; Tan TW; Tsai TH; Chen CC; Hsieh TF; Lee SS; Liu HH; Chen WC; Tang CH

**INSTITUCIÓN / INSTITUTION:** - School of Chinese Medicine, China Medical University, Taichung 404, Taiwan. wgchen@mail.cmu.edu.tw.

**RESUMEN / SUMMARY:** - Prostate cancer is the most commonly diagnosed malignancy in men and shows a predilection for metastasis to the bone. D-pinitol, a 3-methoxy analogue of d-chiro-inositol, was identified as an active principle in soy foods and legumes, and it has been proven to induce tumor apoptosis and metastasis of cancer cells. In this study, we investigated the anti-metastasis effects of D-pinitol in human prostate cancer cells. We found that D-pinitol reduced the migration and the invasion of prostate cancer cells (PC3 and DU145) at noncytotoxic concentrations. Integrins are the major adhesive molecules in mammalian cells and have been associated with the metastasis of cancer cells. Treatment of prostate cancer cells with D-pinitol reduced mRNA and cell surface expression of alphavbeta3 integrin. In addition, D-pinitol exerted its inhibitory effects by reducing focal adhesion kinase (FAK) phosphorylation, c-Src kinase activity and NF-kB activation. Thus, D-pinitol may
be a novel anti-metastasis agent for the treatment of prostate cancer metastasis.

[1591]
**TÍTULO / TITLE:** EZH2, an epigenetic driver of prostate cancer.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**AUTORES / AUTHORS:** Yang YA; Yu J
**INSTITUCIÓN / INSTITUTION:** Division of Hematology/Oncology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, 60611, USA.
**RESUMEN / SUMMARY:** The histone methyltransferase EZH2 has been in the limelight of the field of cancer epigenetics for a decade now since it was first discovered to exhibit an elevated expression in metastatic prostate cancer. It persists to attract much scientific attention due to its important role in the process of cancer development and its potential of being an effective therapeutic target. Thus here we review the dysregulation of EZH2 in prostate cancer, its function, upstream regulators, downstream effectors, and current status of EZH2-targeting approaches. This review therefore provides a comprehensive overview of EZH2 in the context of prostate cancer.

[1592]
**TÍTULO / TITLE:** Concurrent bladder lymphoma and bladder cancer presenting as metastatic bladder cancer.
**RESUMEN / SUMMARY:** Enlace al Resumen / Link to its Summary

**AUTORES / AUTHORS:** Kim JH; Shim JS; Noh TI; Ahn HJ; Bae JH; Park JY
**INSTITUCIÓN / INSTITUTION:** Department of Urology, Soon Chun Hyang University Seoul Hospital, Soon Chun Hyang University College of Medicine, Seoul, Korea.
**RESUMEN / SUMMARY:** Malignant lymphoma of the bladder is a rare lesion, representing approximately 0.2% of the primary lesions and approximately 1.8% of the secondary lesions. A disseminated lymphoma presenting as a bladder mass is an infrequent phenomenon. The authors report the case of a 71-year-old patient with concurrent bladder lymphoma and bladder cancer presenting as metastatic bladder cancer. To the best of our knowledge, this is the first report of concurrent bladder lymphoma and bladder cancer.
Intestinal type villous adenoma of the renal pelvis.

Resumen / Summary: Intestinal type villous adenomas are uncommon in the genitourinary tract. Most reported cases have been located in the urinary bladder or urachus. Villous adenoma arising in the renal pelvis or ureter is very rare. We present a case of an 81-year-old female who presented with difficulty voiding and mucosuria. A computed tomography scan identified right-sided hydronephrosis, renal parenchymal atrophy, nonobstructing calculi and a lower pole renal mass. She underwent open right nephrectomy. Histopathologic examination of the kidney revealed an intestinal type villous adenoma of the renal pelvis with high-grade dysplasia and focal areas suspicious for invasive adenocarcinoma. We review the four previously reported cases of intestinal type villous adenoma in the renal pelvis and discuss diagnosis and management of this unusual neoplasm.

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Prostate cancer and sexual function.

Resumen / Summary: Prostate cancer is now ranked fifth in incidence among cancers in Korean adult males. This is attributable to the more Westernized dietary style which increases the morbidity of prostate cancer and the development of cancer diagnostic technologies, such as prostate-specific antigen and advanced medical systems, increasing the rate of prostate cancer diagnosis. Prostate cancer effects include not only erectile dysfunction caused by the disease itself, but also by psychiatric disorders caused by prostate cancer or its treatments. Prostate cancer by itself reduces sexual desire and the frequency of sexual intercourse. Additionally, surgery or hormonal therapy to block testosterone further increases the frequency of erectile dysfunction.
Erectile dysfunction following radical prostatectomy is primarily attributable to nerve injury caused by intraoperative nerve traction, thermal injury, ischemic injury, and local inflammatory reactions. Additionally, the absence of nocturnal penile tumescence causes persistent hypoxia of the corpus cavernosum, which, secondarily, causes anatomical and functional changes in the corpus cavernosum. Preservation of erectile function is one of the most significant issues for patients with local prostate cancer. Erectile dysfunction following radical prostatectomy is known to have various prognoses, depending on preservation of the neurovascular bundle, patient age, and preoperative erectile status. Intracavernosal injections, PDE5 inhibitors, and penile rehabilitation therapy using a vacuum constriction device after radical prostatectomy are known to improve the recovery of erectile function. Recently, testosterone replacement therapy has also drawn attention as a treatment method.

[1595]
**TÍTULO / TITLE:** - Focal xanthogranulomatous pyelonephritis presenting as renal tumor.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary

[1596]
**TÍTULO / TITLE:** - Defining the threshold for significant versus insignificant prostate cancer.
**RESUMEN / SUMMARY:** - Enlace al Resumen / Link to its Summary
surveillance is now becoming the favoured strategy for deferring active
treatment in men diagnosed with low-risk prostate cancer and reducing their risk
of overtreatment. Almost all eligibility criteria for active surveillance refer to a
strict pathological definition of insignificant prostate cancer, based on two
landmark studies published about 20 years ago. However, current
epidemiological data suggest that this original pathological definition of
insignificant prostate cancer is too restrictive. In addition, the International
Society of Urological Pathology (ISUP) 2005 modification to the Gleason
grading system might have resulted in a marked upgrading of biopsy-diagnosed
prostate cancers, reducing the number of men eligible for active surveillance.
An updated definition of insignificant prostate cancer should reflect the optimal
trade-off between reducing the risk of underestimating a significant prostate
cancer and including as many men as possible in active surveillance
programmes.

[1597]
TÍTULO / TITLE: - Hypoxia, notch signalling, and prostate cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
10.1038/nrurol.2013.110.
AUTORES / AUTHORS: - Marignol L; Rivera-Figueroa K; Lynch T; Hollywood D
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Street, Dublin 8, Ireland.
RESUMEN / SUMMARY: - The notch signalling pathway is involved in
differentiation, proliferation, angiogenesis, vascular remodelling, and apoptosis.
Deregulated expression of notch receptors, ligands, and targets is observed in
many solid tumours, including prostate cancer. Hypoxia is a common feature of
prostate tumours, leading to increased gene instability, reduced treatment
response, and increased tumour aggressiveness. The notch signalling pathway
is known to regulate vascular cell fate and is responsive to hypoxia-inducible
factors. Evidence to date suggests similar, therapeutically exploitable,
behaviour of notch-activated and hypoxic prostate cancer cells.

[1598]
TÍTULO / TITLE: - Urinary PGE-M: A Promising Cancer Biomarker.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
AUTORES / AUTHORS: - Marignol L; Rivera-Figueroa K; Lynch T; Hollywood D
INSTITUCIÓN / INSTITUTION: - Radiation and Urologic Oncology, Prostate
Molecular Oncology Research Group, Academic Unit of Clinical and Molecular
Oncology, Trinity College Dublin, Trinity Centre for Health Sciences, James’s
Street, Dublin 8, Ireland.
RESUMEN / SUMMARY: - The notch signalling pathway is involved in
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Deregulated expression of notch receptors, ligands, and targets is observed in
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response, and increased tumour aggressiveness. The notch signalling pathway
is known to regulate vascular cell fate and is responsive to hypoxia-inducible
factors. Evidence to date suggests similar, therapeutically exploitable,
behaviour of notch-activated and hypoxic prostate cancer cells.
Cancer prevention, early diagnosis, and targeted therapies are the keys to success in better cancer control and treatment. A big challenge remains to identify biomarkers for predicting who may have higher cancer risk and are able to respond to certain chemopreventive agents as well as for assessing a patient’s response during treatment. Although a large body of evidence indicates that chronic inflammation is a risk factor for cancer, it is unclear whether inflammatory biomarkers can be used to predict cancer risk, progression, and death. Considering the importance of the proinflammatory COX-2-derived prostaglandin E2 (PGE2) in inflammation and cancer, Morris and colleagues found that urinary PGE-M is positively associated with obesity, smoking, and lung metastases in patients with breast cancer (4). Along the same lines, Kim and colleagues showed a potential association between urinary PGE-M and breast cancer risk in postmenopausal women (beginning on page 511). In agreement with previous reports, their findings indicate that urinary PGE-M may serve as a promising biomarker for prognosticating cancer risk and disease progression. Cancer Prev Res; 6(6); 507-10. ©2013 AACR.

“We Remain Very Much the Second Sex”: The Constructions of Prostate Cancer in Popular News Magazines, 2000-2010.

Informed by social constructionism, biomedicalization, and a feminist framework, a discourse analysis was performed on 31 popular news articles published in North America between 2000 and 2010. The magazines construct prostate cancer in a gendered manner. Its construction is rooted in themes that are related to discussions of biology, prostate cancer as a heterosexual problem, the responsibilization of health and masculinity. Through these constructions, the popular news articles reinforce dominant ideals and performances of hegemonic masculinity and male sexuality, traditional femininity, and heteronormativity. While reinforcing such ideals, the prevention, treatment, and knowledge of prostate cancer is constructed as the responsibility of individual men. This study reveals that the articles favor discussions of
heteronormativity and hegemonic masculinity over racism, rendering health inequalities silent.