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Artículos originales (todos) * Original articles (all)**

Pancreatic cancer.

October / November 2013

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[1]

TÍTULO / TITLE: - Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial.

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

REVISTA / JOURNAL: - JAMA. 2013 Oct 9;310(14):1473-81. doi: 10.1001/jama.2013.279201.

●● Enlace al texto completo (gratuito o de pago) 1001/jama.2013.279201

AUTORES / AUTHORS: - Oettle H; Neuhaus P; Hochhaus A; Hartmann JT; Gellert K; Ridwelski K; Niedergethmann M; Zulke C; Fahlke J; Arning MB; Sinn M; Hinke A; Riess H

INSTITUCIÓN / INSTITUTION: - Medizinische Klinik mit Schwerpunkt Hamatologie, Onkologie und Tumorimmunologie, Charite-Universitatsmedizin Berlin, Berlin, Germany. helmut.oettle@charite.de

RESUMEN / SUMMARY: - IMPORTANCE: The prognosis for patients with pancreatic cancer is poor, even after resection with curative intent. Gemcitabine-based chemotherapy is standard treatment for advanced pancreatic cancer, but its effect on survival in the adjuvant setting has not been demonstrated. OBJECTIVE: To analyze whether previously reported improvement in disease-free survival with adjuvant gemcitabine therapy translates into improved overall survival. DESIGN, SETTING, AND PATIENTS: CONKO-001 (Charite Onkologie 001), a multicenter, open-label, phase 3 randomized trial to evaluate the efficacy and toxicity of gemcitabine in patients with pancreatic cancer after complete tumor resection. Patients with macroscopically completely removed pancreatic cancer entered the study between July 1998 and December 2004 in 88 hospitals in Germany and Austria. Follow-up ended in September 2012. INTERVENTIONS: After stratification for tumor stage, nodal status,

and resection status, patients were randomly assigned to either adjuvant gemcitabine treatment (1g/m2 d 1, 8, 15, q 4 weeks) for 6 months or to observation alone. MAIN OUTCOMES AND MEASURES: The primary end point was disease-free survival. Secondary end points included treatment safety and overall survival, with overall survival defined as the time from date of randomization to death. Patients lost to follow-up were censored on the date of their last follow-up. RESULTS: A total of 368 patients were randomized, and 354 were eligible for intention-to-treat-analysis. By September 2012, 308 patients (87.0% [95% CI, 83.1%-90.1%]) had relapsed and 316 patients (89.3% [95% CI, 85.6%-92.1%]) had died. The median follow-up time was 136 months. The median disease-free survival was 13.4 (95% CI, 11.6-15.3) months in the treatment group compared with 6.7 (95% CI, 6.0-7.5) months in the observation group (hazard ratio, 0.55 [95% CI, 0.44-0.69]; P < .001). Patients randomized to adjuvant gemcitabine treatment had prolonged overall survival compared with those randomized to observation alone (hazard ratio, 0.76 [95% CI, 0.61-0.95]; P = .01), with 5-year overall survival of 20.7% (95% CI, 14.7%-26.6%) vs 10.4% (95% CI, 5.9%-15.0%), respectively, and 10-year overall survival of 12.2% (95% CI, 7.3%-17.2%) vs 7.7% (95% CI, 3.6%-11.8%). CONCLUSIONS AND RELEVANCE: Among patients with macroscopic complete removal of pancreatic cancer, the use of adjuvant gemcitabine for 6 months compared with observation alone resulted in increased overall survival as well as disease-free survival. These findings provide strong support for the use of gemcitabine in this setting. TRIAL REGISTRATION: isrctn.org Identifier: ISRCTN34802808.

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[2]

TÍTULO / TITLE: - Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine.

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

REVISTA / JOURNAL: - N Engl J Med. 2013 Oct 31;369(18):1691-703. doi: 10.1056/NEJMoa1304369. Epub 2013 Oct 16.

●● Enlace al texto completo (gratuito o de pago) 1056/NEJMoa1304369

AUTORES / AUTHORS: - Von Hoff DD; Ervin T; Arena FP; Chiorean EG; Infante J; Moore M; Seay T; Tjulandin SA; Ma WW; Saleh MN; Harris M; Reni M; Dowden S; Laheru D; Bahary N; Ramanathan RK; Tabernero J; Hidalgo M; Goldstein D; Van Cutsem E; Wei X; Iglesias J; Renschler MF

INSTITUCIÓN / INSTITUTION: - From the Translational Genomics Research Institute, Phoenix, and Virginia G. Piper Cancer Center, Scottsdale - both in Arizona (D.D.V.H., R.K.R.); Cancer Specialists, Fort Myers, FL (T.E.); Arena Oncology Associates, Lake Success (F.P.A.), and Roswell Park Cancer Institute, Buffalo (W.W.M.) - both in New York; University of Washington, Seattle (E.G.C.); Sarah Cannon Research Institute-Tennessee Oncology, Nashville (J. Infante); Princess Margaret Hospital, Toronto (M.M.); Atlanta Cancer Care (T.S.) and Georgia Cancer Specialists (M.N.S.) - both in Atlanta; Blokhin Cancer Research Center, Moscow (S.A.T.); Southern Health, East Bentleigh, VIC (M.H.), Prince of Wales Hospital, Sydney (D.G.), and Bionomics, Thebarton, SA (J. Iglesias) - all in Australia; San Raffaele Scientific Institute, Milan (M.R.); Tom Baker Cancer Centre, Calgary, AB, Canada (S.D.); Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore (D.L.); University of Pittsburgh Medical Center, Pittsburgh (N.B.); Vall d'Hebron University Hospital,

Universitat Autonoma de Barcelona, Barcelona (J.T.); Centro Integral Oncologico Clara Campal, Madrid (M.H.); University Hospitals Leuven and Katholieke Universiteit Leuven, Leuven, Belgium (E.V.C.); and Celgene, Summit, NJ (X.W., M.F.R.).

RESUMEN / SUMMARY: - BACKGROUND: In a phase 1-2 trial of albumin-bound paclitaxel (nab-paclitaxel) plus gemcitabine, substantial clinical activity was noted in patients with advanced pancreatic cancer. We conducted a phase 3 study of the efficacy and safety of the combination versus gemcitabine monotherapy in patients with metastatic pancreatic cancer. METHODS: We randomly assigned patients with a Karnofsky performance-status score of 70 or more (on a scale from 0 to 100, with higher scores indicating better performance status) to nab-paclitaxel (125 mg per square meter of body-surface area) followed by gemcitabine (1000 mg per square meter) on days 1, 8, and 15 every 4 weeks or gemcitabine monotherapy (1000 mg per square meter) weekly for 7 of 8 weeks (cycle 1) and then on days 1, 8, and 15 every 4 weeks (cycle 2 and subsequent cycles). Patients received the study treatment until disease progression. The primary end point was overall survival; secondary end points were progression-free survival and overall response rate. RESULTS: A total of 861 patients were randomly assigned to nab-paclitaxel plus gemcitabine (431 patients) or gemcitabine (430). The median overall survival was 8.5 months in the nab-paclitaxel-gemcitabine group as compared with 6.7 months in the gemcitabine group (hazard ratio for death, 0.72; 95% confidence interval [CI], 0.62 to 0.83; P<0.001). The survival rate was 35% in the nab-paclitaxel-gemcitabine group versus 22% in the gemcitabine group at 1 year, and 9% versus 4% at 2 years. The median progression-free survival was 5.5 months in the nab-paclitaxel-gemcitabine group, as compared with 3.7 months in the gemcitabine group (hazard ratio for disease progression or death, 0.69; 95% CI, 0.58 to 0.82; P<0.001); the response rate according to independent review was 23% versus 7% in the two groups (P<0.001). The most common adverse events of grade 3 or higher were neutropenia (38% in the nab-paclitaxel-gemcitabine group vs. 27% in the gemcitabine group), fatigue (17% vs. 7%), and neuropathy (17% vs. 1%). Febrile neutropenia occurred in 3% versus 1% of the patients in the two groups. In the nab-paclitaxel-gemcitabine group, neuropathy of grade 3 or higher improved to grade 1 or lower in a median of 29 days. CONCLUSIONS: In patients with metastatic pancreatic adenocarcinoma, nab-paclitaxel plus gemcitabine significantly improved overall survival, progression-free survival, and response rate, but rates of peripheral neuropathy and myelosuppression were increased. (Funded by Celgene; ClinicalTrials.gov number, NCT00844649.).

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[3]

TÍTULO / TITLE: - Randomized, Multicenter, Phase II Study of CO-101 Versus Gemcitabine in Patients With Metastatic Pancreatic Ductal Adenocarcinoma: Including a Prospective Evaluation of the Role of hENT1 in Gemcitabine or CO-101 Sensitivity.

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

REVISTA / JOURNAL: - J Clin Oncol. 2013 Nov 12.

●● Enlace al texto completo (gratuito o de pago) 1200/JCO.2013.51.0826

AUTORES / AUTHORS: - Poplin E; Wasan H; Rolfe L; Raponi M; Ikdahl T; Bondarenko I; Davidenko I; Bondar V; Garin A; Boeck S; Ormanns S; Heinemann V; Bassi C; Evans TR; Andersson R; Hahn H; Picozzi V; Dicker A; Mann E; Voong C; Kaur P; Isaacson J; Allen A

INSTITUCIÓN / INSTITUTION: - Elizabeth Poplin, Cancer Institute of New Jersey, New Brunswick, NJ; Mitch Raponi, Elaina Mann, Cynthia Voong, and Andrew Allen, Clovis Oncology, San Francisco, CA; Hejin Hahn and Vince Picozzi, Virginia Mason Medical Center, Seattle, WA; Adam Dicker, Radiation Therapy Oncology Group, Philadelphia, PA; Jeff Isaacson, Clovis Oncology, Boulder, CO; Harpreet Wasan, Hammersmith Hospital, London; Lindsey Rolfe and Paramjit Kaur, Clovis Oncology UK, Cambridge; T.R. Jeffrey Evans, University of Glasgow, Glasgow, United Kingdom; Tone Ikdahl, Oslo Universitetssykehus, Oslo, Norway; Ihor Bondarenko, Dnipropetrovsk State Medical Academy, Dnipropetrovsk; Volodymyr Bondar, Donetsk Regional Antitumor Center, Donetsk, Ukraine; Irina Davidenko, Clinical Oncology Center 1, Krasnodar; August Garin, Blokhin Russian Cancer Research Center, Moscow, Russia; Stefan Boeck, Steffen Ormanns, and Volker Heinemann, Ludwig-Maximilians-University of Munich, Munich, Germany; Claudio Bassi, Ospedale Policlinico G.B. Rossi, Verona, Italy; and Roland Andersson, Lund University, Lund, Sweden.

RESUMEN / SUMMARY: - PURPOSE: Gemcitabine requires transporter proteins to cross cell membranes. Low expression of human equilibrative nucleoside transporter-1 (hENT1) may result in gemcitabine resistance in pancreatic ductal adenocarcinoma (PDAC). CO-101, a lipid-drug conjugate of gemcitabine, was rationally designed to enter cells independently of hENT1. We conducted a randomized controlled trial to determine whether CO-101 improved survival versus gemcitabine in patients with metastatic PDAC (mPDAC) with low hENT1. The study also tested the hypothesis that gemcitabine is more active in patients with mPDAC tumors with high versus low hENT1 expression. PATIENTS AND METHODS: Patients were randomly assigned to CO-101 or gemcitabine, after providing a metastasis sample for blinded hENT1 assessment. An immunohistochemistry test measuring tumor hENT1 was developed. To dichotomize the population, an hENT1 cutoff value was defined using primary PDAC samples from an adjuvant trial, and a high/low cutoff was applied. The primary end point was overall survival (OS) in the low hENT1 subgroup. RESULTS: Of 367 patients enrolled, hENT1 status was measured in 358 patients (97.5%). Two hundred thirty-two (64.8%) of 358 patients were hENT1 low. There was no difference in OS between treatments in the low hENT1 subgroup or overall, with hazard ratios (HRs) of 0.994 (95% CI, 0.746 to 1.326) and 1.072 (95% CI, 0.856 to 1.344), respectively. The toxicity profiles in both arms were similar. Within the gemcitabine arm, there was no difference in survival between the high and low hENT1 subgroups (HR, 1.147; 95% CI, 0.809 to 1.626). CONCLUSION: CO-101 is not superior to gemcitabine in patients with mPDAC and low tumor hENT1. Metastasis hENT1 expression did not predict gemcitabine outcome.

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[4]

TÍTULO / TITLE: - Randomized double-blinded, placebo-controlled phase II trial of simvastatin and gemcitabine in advanced pancreatic cancer patients.

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

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Oct 27.

●● Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2328-1

AUTORES / AUTHORS: - Hong JY; Nam EM; Lee J; Park JO; Lee SC; Song SY; Choi SH; Heo JS; Park SH; Lim HY; Kang WK; Park YS

INSTITUCIÓN / INSTITUTION: - Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong Gangnam-gu, Seoul, 135-710, Korea.

RESUMEN / SUMMARY: - BACKGROUND: Statins have potential antineoplastic properties via arrest of cell-cycle progression and induction of apoptosis. A previous study demonstrated in vitro and in vivo antineoplastic synergism between statins and gemcitabine. The present randomized, double-blinded, phase II trial compared the efficacy and safety of gemcitabine plus simvastatin (GS) with those of gemcitabine plus placebo (GP) in patients with locally advanced and metastatic pancreatic cancer. METHODS: Patients were randomly assigned to receive a 3-week regimen with GS (gemcitabine 1,000 mg/m2 on days 1, 8, and 15 plus simvastatin 40 mg once daily) or GP (gemcitabine 1,000 mg/m2 on days 1, 8, and 15 plus placebo). The primary end point was time to progression (TTP). RESULTS: Between December 2008 and April 2012, 114 patients were enrolled. The median TTP was not significantly different between the two arms, being 2.4 months (95 % CI 0.7-4.1 months) and 3.6 months (95 % CI 3.1-4.1 months) in the GS and GP arms, respectively (P = 0.903). The overall disease control rate was 39.7 % (95 % CI 12.2-33.8 %) and 57.1 % (95 % CI 19.8-44.2 %) in the GS and GP arms, respectively (P = 0.09). The 1-year expected survival rates were similar (27.7 and 31.7 % in the GS and GP arms, respectively; P = 0.654). Occurrence of grade 3 or 4 adverse events was similar in both arms, and no patients had rhabdomyolysis. CONCLUSIONS: Adding low-dose simvastatin to gemcitabine in advanced pancreatic cancer does not provide clinical benefit, although it also does not result in increased toxicity. Given the emerging role of statins in overcoming resistance to anti-EGFR treatment, further studies are justified to evaluate the efficacy and safety of combined simvastatin and anti-EGFR agents, such as erlotinib or cetuximab, plus gemcitabine for treating advanced pancreatic cancer.

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[5]

TÍTULO / TITLE: - Loss of DAXX and ATRX are Associated with Chromosome Instability and Reduced Survival of Patients with Pancreatic Neuroendocrine Tumors.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Oct 19. pii: S0016-5085(13)01494-7. doi: 10.1053/j.gastro.2013.10.020.

●● Enlace al texto completo (gratuito o de pago) 1053/j.gastro.2013.10.020

AUTORES / AUTHORS: - Marinoni I; Kurrer AS; Vassella E; Dettmer M; Rudolph T; Banz V; Hunger F; Pasquinelli S; Speel EJ; Perren A

INSTITUCIÓN / INSTITUTION: - Institute of Pathology, University of Bern, Switzerland.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Sporadic pancreatic neuroendocrine tumors (pNETs) are rare and genetically heterogeneous. Chromosome instability (CIN) has been detected in pNETs from patients with poor outcomes, but no specific genetic factors have been associated with CIN. Mutations in DAXX or ATRX (which both encode proteins involved in chromatin remodeling) have been detected in 40% of pNETs, in association with activation of alternative lengthening of telomeres. We investigated whether loss of DAXX or ATRX, and consequent alternative lengthening of telomeres, are related to CIN in pNETs. We also assessed whether loss of DAXX or ATRX is associated with specific phenotypes of pNETs. METHODS: We collected well-differentiated primary pNET samples from 142 patients at the University

Hospital Zurich and 101 patients at the University Hospital Bern, Switzerland. Clinical follow-up data were obtained for 149 patients from general practitioners and tumor registries. The tumors were reclassified into 3 groups according to the 2010 WHO classification. Samples were analyzed by immunohistochemistrey and telomeric fluorescence in situ hybridization. We correlated loss of DAXX, or ARTX expression, and activation of alternative lengthening of telomeres with data from comparative genomic hybridization array studies, as well as with clinical and pathology features of the tumors and relapse and survival data. RESULTS: Loss of DAXX or ARTX protein and alternative lengthening of telomeres were associated with CIN in pNETs. Furthermore, loss of DAXX or ARTX correlated with tumor stage and metastasis, reduced time of relapse-free survival, and decreased time of tumor-associated survival. CONCLUSIONS: Loss of DAXX or ARTX is associated with CIN in pNETs and shorter survival times of patients. These results support the hypothesis that DAXX- and ATRX-negative tumors are a more aggressive subtype of pNET, and could lead to identification of strategies to target CIN in pancreatic tumors.

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[6]

TÍTULO / TITLE: - Low CHD5 expression activates the DNA damage response and predicts poor outcome in patients undergoing adjuvant therapy for resected pancreatic cancer.

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

REVISTA / JOURNAL: - Oncogene. 2013 Nov 25. doi: 10.1038/onc.2013.488.

●● Enlace al texto completo (gratuito o de pago) 1038/onc.2013.488

AUTORES / AUTHORS: - Hall WA; Petrova AV; Colbert LE; Hardy CW; Fisher SB; Saka B; Shelton JW; Warren MD; Pantazides BG; Gandhi K; Kowalski J; Kooby DA; El-Rayes BF; Staley CA 3rd; Volkan Adsay N; Curran WJ; Landry JC; Maithel SK; Yu DS

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Winship Cancer Institute, Emory University, Atlanta, GA, USA.

RESUMEN / SUMMARY: - The DNA damage response (DDR) promotes genome integrity and serves as a cancer barrier in precancerous lesions but paradoxically may promote cancer survival. Genes that activate the DDR when dysregulated could function as useful biomarkers for outcome in cancer patients. Using a siRNA screen in human pancreatic cancer cells, we identified the CHD5 tumor suppressor as a gene, which, when silenced, activates the DDR. We evaluated the relationship of CHD5 expression with DDR activation in human pancreatic cancer cells and the association of CHD5 expression in 80 patients with resected pancreatic adenocarcinoma (PAC) by immunohistochemical analysis with clinical outcome. CHD5 depletion and low CHD5 expression in human pancreatic cancer cells lead to increased H2AX-Ser139 and CHK2-Thr68 phosphorylation and accumulation into nuclear foci. On Kaplan-Meier log-rank survival analysis, patients with low CHD5 expression had a median recurrence-free survival (RFS) of 5.3 vs 15.4 months for patients with high CHD5 expression (P=0.03). In 59 patients receiving adjuvant chemotherapy, low CHD5 expression was associated with decreased RFS (4.5 vs 16.3 months; P=0.001) and overall survival (OS) (7.2 vs 21.6 months; P=0.003). On multivariate Cox regression analysis, low CHD5 expression remained associated with worse OS (HR: 3.187 (95% CI: 1.49-6.81); P=0.003) in patients undergoing adjuvant chemotherapy. Thus, low CHD5 expression activates the DDR and predicts for worse OS in patients with resected PAC receiving

adjuvant chemotherapy. Our findings support a model in which dysregulated expression of tumor suppressor genes that induce DDR activation can be utilized as biomarkers for poor outcome.Oncogene advance online publication, 25 November 2013; doi:10.1038/onc.2013.488.

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[7]
TÍTULO / TITLE: - Comparison of response evaluation in patients with gastroenteropancreatic and thoracic neuroendocrine tumors after treatment with [177Lu-DOTA0,Tyr3]octreotate.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Nucl Med. 2013 Oct;54(10):1689-96. doi: 10.2967/jnumed.112.117408.
●● Enlace al texto completo (gratuito o de pago) 2967/jnumed.112.117408
AUTORES / AUTHORS: - van Vliet EI; Krenning EP; Teunissen JJ; Bergsma H; Kam BL; Kwekkeboom DJ
INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, Erasmus MC, University Medical Center, Rotterdam, The Netherlands.
RESUMEN / SUMMARY: - Response Evaluation Criteria In Solid Tumors (RECIST) (unidimensional), Southwest Oncology Group (SWOG) solid tumor response criteria (bidimensional), and their modified variants are commonly used in the tumor response assessment after treatment of gastroenteropancreatic and thoracic neuroendocrine tumors (NETs). In the current study, RECIST, SWOG criteria, modified RECIST (mRECIST), and modified SWOG (mSWOG) criteria were compared in patients with NETs treated with [(177)Lu-DOTA(0),Tyr(3)]octreotate ((177)Lu-octreotate). METHODS: Two-hundred sixty-eight Dutch patients with NETs who had been treated with (177)Lu-octreotate between January 2000 and April 2007 were studied. CT or MR imaging scans were analyzed using RECIST, SWOG criteria, mRECIST, and mSWOG criteria (including the tumor response class minor response [decrease of 13%-30% for mRECIST and 25%-50% for mSWOG]). The outcomes were correlated with progression-free survival (PFS) and overall survival (OS). RESULTS: Eleven patients had an unknown tumor response and were excluded. The rates of objective response (OR) (complete response + partial response [+minor response for mRECIST/mSWOG]), stable disease, and progressive disease (PD) were 28%, 49%, and 24%, respectively, according to RECIST; 25%, 49%, and 26%, respectively, according to SWOG; 44%, 33%, and 24%, respectively, according to mRECIST; and 45%, 29%, and 26%, respectively, according to mSWOG. In patients who had OR, stable disease, or PD, the median PFS was 26-30, 27-34, and 8 mo, respectively, with any of the 4 response criteria. In patients who had OR, stable disease, or PD, the median OS was 55-57, 56-74, and 11-12 mo, respectively, with any of the 4 response criteria. Subanalyses for patients who had progression before treatment start were comparable. CONCLUSION: Patients with PD as treatment outcome had significantly shorter PFS and OS than patients with an OR or stable disease with all 4 scoring systems. PFS and OS were comparable for patients with tumor regression and stable disease. The addition of the response class minor response did not improve the correlation with PFS and OS. The 4 scoring systems gave comparable results in terms of PFS and OS per categorized outcome.

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[8]

TÍTULO / TITLE: - Nuclear Death Receptor TRAILR2 Inhibits Maturation of Let-7 and Promotes Proliferation of Pancreatic and Other Tumor cells.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Oct 9. pii: S0016-5085(13)01429-7. doi: 10.1053/j.gastro.2013.10.009.

●● Enlace al texto completo (gratuito o de pago) 1053/j.gastro.2013.10.009

AUTORES / AUTHORS: - Haselmann V; Kurz A; Bertsch U; Hubner S; Olempska-Muller M; Fritsch J; Hasler R; Pickl A; Fritsche H; Annewanter F; Engler C; Fleig B; Bernt A; Roder C; Schmidt H; Gelhaus C; Hauser C; Egberts JH; Heneweer C; Rohde AM; Boger C; Knippschild U; Rocken C; Adam D; Walczak H; Schutze S; Janssen O; Wulczyn FG; Wajant H; Kalthoff H; Trauzold A

INSTITUCIÓN / INSTITUTION: - Division of Molecular Oncology, Institute for Experimental Cancer Research, University of Kiel, Kiel, Germany.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: TRAILR1 (TNFRSF10A) and TRAILR2 (TNFRSF10B) on the plasma membrane bind ligands that activate apoptotic and other signaling pathways. Cancer cells also might have TRAILR2 in the cytoplasm or nucleus, although little is known about its activities in these locations. We investigated the functions of nuclear TRAILR2 in cancer cell lines. METHODS: Proteins that interact with TRAILR2 initially were identified in pancreatic cancer cells by immunoprecipitation, mass spectrometry, and immunofluorescence analyses. Findings were validated in colon, renal, lung, and breast cancer cells. Functions of TRAILR2 were determined from small interfering RNA knockdown, real-time polymerase chain reaction, Drosha-activity, microRNA array, proliferation, differentiation, and immunoblot experiments. We assessed the effects of TRAILR2 overexpression or knockdown in human pancreatic ductal adenocarcinoma (PDAC) cells and their ability to form tumors in mice. We also analyzed levels of TRAILR2 in sections of PDACs and non-neoplastic peritumoral ducts from patients. RESULTS: TRAILR2 was found to interact with the core microprocessor components Drosha and DGCR8 and the associated regulatory proteins p68, hnRNPA1, NF45, and NF90 in nuclei of PDAC and other tumor cells. Knockdown of TRAILR2 increased Drosha-mediated processing of the let-7 microRNA precursor primary let-7 (resulting in increased levels of mature let-7), reduced levels of the let-7 targets (LIN28B and HMGA2), and inhibited cell proliferation. PDAC tissues from patients had higher levels of nuclear TRAILR2 than non-neoplastic pancreatic tissue, which correlated with increased nuclear levels of HMGA2 and poor outcomes. Knockdown of TRAILR2 in PDAC cells slowed their growth as orthotopic tumors in mice. Reduced nuclear levels of TRAILR2 in cultured pancreatic epithelial cells promoted their differentiation. CONCLUSIONS: Nuclear TRAILR2 inhibits maturation of the microRNA let-7 in pancreatic cancer cell lines and increases their proliferation. Pancreatic tumor samples have increased levels of nuclear TRAILR2, which correlate with poor outcome of patients. These findings indicate that in the nucleus, death receptors can function as tumor promoters and might be therapeutic targets.

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[9]

TÍTULO / TITLE: - A phase I trial of combination therapy using gemcitabine and S-1 concurrent with full-dose radiation for resectable pancreatic cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Nov 21.
●● Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2357-9
AUTORES / AUTHORS: - Eguchi H; Nagano H; Kobayashi S; Kawamoto K; Wada H; Hama N; Tomimaru Y; Akita H; Sakai D; Satoh T; Kudo T; Isohashi F; Mori M; Doki Y
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Graduate School of Medicine, Osaka University, 2-2 Yamadaoka E-2, Suita 565-0871, Osaka, Japan, heguchi@gesurg.med.osaka-u.ac.jp.
RESUMEN / SUMMARY: - PURPOSE: Use of the fourth-generation oral fluoropyrimidine S-1 together with gemcitabine has shown striking anticancer effects. In this single-arm phase I trial of preoperative combination therapy using gemcitabine and S-1 concurrently with radiotherapy, we verified the safety and feasibility and determined the maximum-tolerated dose of each drug in patients with resectable pancreatic cancer. METHODS: A standard 3+3 dose escalation scheme was used. Patients with cytologically or histologically proven resectable pancreatic ductal adenocarcinoma were administered 30-min intravenous gemcitabine infusions on days 1, 8, 22, and 29 and S-1 orally on days 1-5, 8-12, 22-26, and 29-33. A total radiation dose of 50.4 Gy (1.8 Gy/day, 5 times per week, 28 fractions) was concurrently delivered. Surgical exploration was scheduled 4-7 weeks after the final radiation fraction. RESULTS: Twenty-one patients were enrolled. No treatment-related deaths occurred during this study. Recommended doses were determined to be 80 mg/m2 of S-1 daily and 1,000 mg/m2 of gemcitabine. CA19-9 was reduced to <50 % of baseline values in 12 (75 %) of 16 measurable patients. Nineteen of 21 enrolled patients successfully underwent surgical resection. CONCLUSIONS: Preoperative chemoradiotherapy consisting of gemcitabine and S-1 concurrent with full-dose radiation is feasible and well tolerated.

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[10]
TÍTULO / TITLE: - Defining Optimum Treatment of Patients With Pancreatic Adenocarcinoma Using Regret-Based Decision Curve Analysis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Ann Surg. 2013 Oct 28.
●● Enlace al texto completo (gratuito o de pago)
1097/SLA.0000000000000310
AUTORES / AUTHORS: - Hernandez JM; Tsalatsanis A; Humphries LA; Miladinovic B; Djulbegovic B; Velanovich V
INSTITUCIÓN / INSTITUTION: - *Department of Surgery, Division of General Surgery, University of South Florida, Tampa, FL; daggerCenter for Evidence-Based Medicine, University of South Florida, Tampa, FL; double daggerDepartment of Internal Medicine, Division of Evidence-Based Medicine, Tampa, FL; and section signDepartment of Hematology and Health Outcomes and Behavior, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL.
RESUMEN / SUMMARY: - OBJECTIVES:: To use regret decision theory methodology to assess three treatment strategies in pancreatic adenocarcinoma. BACKGROUND:: Pancreatic adenocarcinoma is uniformly fatal without operative intervention. Resection can prolong survival in some patients; however, it is associated with significant morbidity and mortality. Regret theory serves as a novel framework linking both rationality and intuition to determine the optimal course for physicians facing difficult

decisions related to treatment. METHODS:: We used the Cox proportional hazards model to predict survival of patients with pancreatic adenocarcinoma and generated a decision model using regret-based decision curve analysis, which integrates both the patient's prognosis and the physician's preferences expressed in terms of regret associated with a certain action. A physician's treatment preferences are indicated by a threshold probability, which is the probability of death/survival at which the physician is uncertain whether or not to perform surgery. The analysis modeled 3 possible choices: perform surgery on all patients; never perform surgery; and act according to the prediction model. RESULTS:: The records of 156 consecutive patients with pancreatic adenocarcinoma were retrospectively evaluated by a single surgeon at a tertiary referral center. Significant independent predictors of overall survival included preoperative stage [P = 0.005; 95% confidence interval (CI), 1.19-2.27], vitality (P < 0.001; 95% CI, 0.96-0.98), daily physical function (P < 0.001; 95% CI, 0.97-0.99), and pathological stage (P < 0.001; 95% CI, 3.06-16.05). Compared with the "always aggressive" or "always passive" surgical treatment strategies, the survival model was associated with the least amount of regret for a wide range of threshold probabilities. CONCLUSIONS:: Regret-based decision curve analysis provides a novel perspective for making treatment-related decisions by incorporating the decision maker's preferences expressed as his or her estimates of benefits and harms associated with the treatment considered.

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[11]

TÍTULO / TITLE: - Validation of C-reactive protein levels as a prognostic indicator for survival in a large cohort of pancreatic cancer patients.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 7. doi: 10.1038/bjc.2013.701.

●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.701

AUTORES / AUTHORS: - Szkandera J; Stotz M; Absenger G; Stojakovic T; Samonigg H; Kornprat P; Schaberl-Moser R; Alzoughbi W; Lackner C; Ress AL; Seggewies FS; Gerger A; Hoefler G; Pichler M

INSTITUCIÓN / INSTITUTION: - Division of Clinical Oncology, Department of Medicine, Medical University of Graz, Auenbruggerplatz 15, 8036 Graz, Austria.

RESUMEN / SUMMARY: - Background:Recent evidence indicates that the host inflammatory response has an important role in the tumour progression. Elevated C-reactive protein (CRP) levels have been previously associated with poor prognosis in several cancer types including small-scale studies in pancreatic cancer (PC) patients. The purpose of the present study was to validate the prognostic impact of plasma CRP levels at date of diagnosis on cancer-specific survival (CSS) in a large cohort of PC patients.Methods:Data from 474 consecutive patients with adenocarcinoma of the pancreas, treated between 2004 and 2012 at a single centre, were evaluated retrospectively. CSS was analysed using the Kaplan-Meier method. To evaluate the prognostic significance of plasma CRP levels, univariate and multivariate Cox analyses were applied.Results:High plasma CRP levels at diagnosis were significantly associated with well-established prognostic factors, including high tumour stage and tumour grade and the administration of chemotherapy (P<0.05). In univariate analysis, we observed that a high plasma CRP level was a consistent factor for poor CSS in PC patients (hazard ratio (HR)=2.21; 95% confidence interval (CI)=1.68-2.92, P<0.001). In

multivariate analysis, tumour stage, grade, administration of chemotherapy, a high neutrophil-lymphocyte ratio and the highest quartile of CRP levels (HR=1.60, 95% CI=1.16-2.21; P=0.005) were identified as independent prognostic factors in PC patients.Conclusion:In conclusion, we confirmed a significant association of elevated CRP levels with poor clinical outcome in PC patients. Our results indicate that the plasma CRP level might represent a useful marker for patient stratification in PC management.British Journal of Cancer advance online publication, 7 November 2013; doi:10.1038/bjc.2013.701 www.bjcancer.com.

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[12]

TÍTULO / TITLE: - COUP-TFII in pancreatic adenocarcinoma: Clinical implication for patient survival and tumor progression.

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

REVISTA / JOURNAL: - Int J Cancer. 2013 Oct 1. doi: 10.1002/ijc.28502.

●● Enlace al texto completo (gratuito o de pago) 1002/ijc.28502

AUTORES / AUTHORS: - Polvani S; Tarocchi M; Tempesti S; Mello T; Ceni E; Buccoliero F; D'Amico M; Boddi V; Farsi M; Nesi S; Nesi G; Milani S; Galli A

INSTITUCIÓN / INSTITUTION: - Department of Experimental and Clinical Biomedical Sciences, University of Florence, Firenze, Italy.

RESUMEN / SUMMARY: - Despite the accumulating knowledge of alterations in pancreatic cancer molecular pathways, no substantial improvements in the clinical prognosis have been made and this malignancy continues to be a leading cause of cancer death in the Western World. The orphan nuclear receptor COUP-TFII is a regulator of a wide range of biological processes and it may exert a pro-oncogenic role in cancer cells; interestingly, indirect evidences suggest that the receptor could be involved in pancreatic cancer. The aim of this study was to evaluate the expression of COUP-TFII in human pancreatic tumors and to unveil its role in the regulation of pancreatic tumor growth. We evaluated COUP-TFII expression by immunohistochemistry on primary samples. We analyzed the effect of the nuclear receptor silencing in human pancreatic cancer cells by means of shRNA expressing cell lines. We finally confirmed the in vitro results by in vivo experiments on nude mice. COUP-TFII is expressed in 69% of tested primary samples and correlates with the N1 and M1 status and clinical stage; Kaplan-Meier and Cox regression analysis show that it may be an independent prognostic factor of worst outcome. In vitro silencing of COUP-TFII reduces the cell growth and invasiveness and it strongly inhibits angiogenesis, an effect mediated by the regulation of VEGF-C. In nude mice, COUP-TFII silencing reduces tumor growth by 40%. Our results suggest that COUP-TFII might be an important regulator of the behavior of pancreatic adenocarcinoma, thus representing a possible new target for pancreatic cancer therapy.

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[13]

TÍTULO / TITLE: - Correlation of Smad4 status with outcomes in patients receiving erlotinib combined with adjuvant chemoradiation and chemotherapy after resection for pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Nov 1;87(3):458-9. doi: 10.1016/j.ijrobp.2013.06.2039.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ijrobp.2013.06.2039

AUTORES / AUTHORS: - Herman JM; Fan KY; Wild AT; Wood LD; Blackford AL; Donehower RC; Hidalgo M; Schulick RD; Edil BH; Choti MA; Hruban RH; Pawlik TM; Cameron JL; Laheru DA; Iacobuzio-Donahue CA; Wolfgang CL

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology & Molecular Radiation Sciences, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, Maryland. Electronic address: jherma15@jhmi.edu.

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[14]

TÍTULO / TITLE: - Pancreatic Cancer Death Rates by Race Among US Men and Women, 1970-2009.

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

REVISTA / JOURNAL: - J Natl Cancer Inst. 2013 Nov 20;105(22):1694-700. doi: 10.1093/jnci/djt292. Epub 2013 Nov 7.

●● Enlace al texto completo (gratuito o de pago) 1093/jnci/djt292

AUTORES / AUTHORS: - Ma J; Siegel R; Jemal A

INSTITUCIÓN / INSTITUTION: - Affiliations of authors: Surveillance and Health Services Research program, American Cancer Society (JM, RS, AJ).

RESUMEN / SUMMARY: - BACKGROUND: Few studies have examined trends in pancreatic cancer death rates in the United States, and there have been no studies examining recent trends using age-period-cohort analysis. METHODS: Annual percentage change in pancreatic cancer death rates was calculated for 1970 to 2009 by sex and race among adults aged 35 to 84 years using US mortality data provided by the National Center for Health Statistics and Joinpoint Regression. Age-period-cohort modeling was performed to evaluate the changes in cohort and period effects. All statistical tests were two-sided. RESULTS: In white men, pancreatic cancer death rates decreased by 0.7% per year from 1970 to 1995 and then increased by 0.4% per year through 2009. Among white women, rates increased slightly from 1970 to 1984, stabilized until the late 1990s, then increased by 0.5% per year through 2009. In contrast, the rates among blacks increased between 1970 and the late 1980s (women) or early 1990s (men) and then decreased thereafter. Age-period-cohort analysis showed that pancreatic cancer death risk was highest for the 1900 to 1910 birth cohort in men and the 1920 to 1930 birth cohort in women and there was a statistically significant increase in period effects since the late 1990s in both white men and white women (two-sided Wald test, P < .001). CONCLUSIONS: In the United States, whites and blacks experienced opposite trends in pancreatic cancer death rates between 1970 and 2009 that are largely unexplainable by known risk factors. This study underscores the needs for urgent action to curb the increasing trends of pancreatic cancer in whites and for better understanding of the etiology of this disease.

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[15]

TÍTULO / TITLE: - DCLK1 Marks a Morphologically Distinct Subpopulation of Cells With Stem Cell Properties in Preinvasive Pancreatic Cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Gastroenterology. 2013 Oct 2. pii: S0016-5085(13)01411-X. doi: 10.1053/j.gastro.2013.09.050.

●● Enlace al texto completo (gratuito o de pago) 1053/j.gastro.2013.09.050

AUTORES / AUTHORS: - Bailey JM; Alsina J; Rasheed ZA; McAllister FM; Fu YY; Plentz R; Zhang H; Pasricha PJ; Bardeesy N; Matsui W; Maitra A; Leach SD

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland; The McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: As in other tumor types, progression of pancreatic cancer may require a functionally unique population of cancer stem cells. Although such cells have been identified in many invasive cancers, it is not clear whether they emerge during early or late stages of tumorigenesis. Using mouse models and human pancreatic cancer cell lines, we investigated whether preinvasive pancreatic neoplasia contains a subpopulation of cells with distinct morphologies and cancer stem cell-like properties. METHODS: Pancreatic tissue samples were collected from the KCPdx1, KPCPdx1, and KCiMist1 mouse models of pancreatic intraepithelial neoplasia (PanIN) and analyzed by confocal and electron microscopy, lineage tracing, and fluorescence-activated cell sorting. Subpopulations of human pancreatic ductal adenocarcinoma (PDAC) cells were similarly analyzed and also used in complementary DNA microarray analyses. RESULTS: The microtubule regulator DCLK1 marked a morphologically distinct and functionally unique population of pancreatic cancer-initiating cells. These cells displayed morphological and molecular features of gastrointestinal tuft cells. Cells that expressed DCLK1 also expressed high levels of ATAT1, HES1, HEY1, IGF1R, and ABL1, and manipulation of these pathways in PDAC cell lines inhibited their clonogenic potential. Pharmacological inhibition of gamma-secretase activity reduced the abundance of these cells in murine PanIN in a manner that correlated with inhibition of PanIN progression. CONCLUSIONS: Human PDAC cells and pancreatic neoplasms in mice contain morphologically and functionally distinct subpopulations that have cancer stem cell-like properties. These populations can be identified at the earliest stages of pancreatic tumorigenesis and provide new cellular and molecular targets for pancreatic cancer treatment and/or chemoprevention.

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[16]

TÍTULO / TITLE: - Preparing for Prospective Clinical Trials: A National Initiative of an Excellence Registry for Consecutive Pancreatic Cancer Resections.

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

REVISTA / JOURNAL: - World J Surg. 2013 Oct 12.

●● Enlace al texto completo (gratuito o de pago) 1007/s00268-013-2283-3

AUTORES / AUTHORS: - Gangl O; Sahora K; Kornprat P; Margreiter C; Primavesi F; Bareck E; Schindl M; Langle F; Ofner D; Mischinger HJ; Pratschke J; Gnant M; Fugger R

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Elisabethinen Hospital Linz, Fadingerstrasse 1, 4020, Linz, Austria, odogangl@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: Despite significant improvements in perioperative mortality as well as response rates to multimodality treatment, results after surgical resection of pancreatic adenocarcinoma with respect to long-term

outcomes remain disappointing. Patient recruitment for prospective international trials on adjuvant and neoadjuvant regimens is challenging for various reasons. We set out to assess the preconditions and potential to perform perioperative trials for pancreatic cancer within a well-established Austrian nationwide network of surgical and medical oncologists (Austrian Breast & Colorectal Cancer Study Group). METHODS: From 2005 to 2010 five high-volume centers and one medium-volume center completed standardized data entry forms with 33 parameters (history and patient related data, preoperative clinical staging and work-up, surgical details and intraoperative findings, postoperative complications, reinterventions, reoperations, 30-day mortality, histology, and timing of multimodality treatment). Outside of the study group, in Austria pancreatic resections are performed in three “high-volume” centers (>10 pancreatic resections per year), three “medium-volume” centers (5-10 pancreatic resections per year), and the rest in various low-volume centers (<5 pancreatic resections per year) in Austria. Nationwide data for prevalence of and surgical resections for pancreatic adenocarcinoma were contributed by the National Cancer Registry of Statistics of Austria and the Austrian Health Institute. RESULTS: In total, 492 consecutive patients underwent pancreatic resection for ductal adenocarcinoma. All postoperative complications leading to hospital readmission were treated at the primary surgical department and documented in the database. Overall morbidity and pancreatic fistula rate were 45.5 % and 10.1 %, respectively. Within the entire cohort there were 9.8 % radiological reinterventions and 10.4 % reoperations. Length of stay was 16 days in median (0-209); 12 of 492 patients died within 30 days after operation, resulting in a 30-day mortality rate of 2.4 %. Seven of the total 19 deaths (36.8 %) occurred after 30 days, during hospitalization at the surgical department, resulting in a hospital mortality rate of 3.9 % (19/492). With a standardized histopathological protocol, there were 70 % (21/30) R0 resections, 30 % (9/30) R1 resections, and no R2 resections in Vienna and 62.7 % (32/51) R0 resections, 35.3 % (18/51) R1 resections, and 2 % (1/51) R2 resections in Salzburg. Resection margin status with nonstandardized protocols was classified as R0 in 82 % (339/411), R1 in 16 % (16/411), and R2 in 1.2 % (5/411). Perioperative chemotherapy was administered in 81.1 % of patients (8.3 % neoadjuvant; 68.5 % adjuvant; 4.3 % palliative); chemoradiotherapy (1.6 % neoadjuvant; 3 % adjuvant; 0.2 % palliative), in 4.9 % of patients. The six centers that contributed to this registry initiative provided surgical treatment to 40 % of all Austrian patients, resulting in a median annual recruitment of 85 (51-104) patients for the entire ABCSG-group and a median of 11.8 (0-38) surgeries for each individual department. CONCLUSIONS: Surgical quality data of the ABCSG core pancreatic group are in line with international standards. With continuing centralization the essential potential to perform prospective clinical trials for pancreatic adenocarcinoma is given in Austria. Several protocol proposals aiming at surgical and multimodality research questions are currently being discussed.

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[17]

TÍTULO / TITLE: - Preparing for Prospective Clinical Trials: A National Initiative of an Excellence Registry for Consecutive Pancreatic Cancer Resections.

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

REVISTA / JOURNAL: - World J Surg. 2013 Nov 19.

●● Enlace al texto completo (gratuito o de pago) 1007/s00268-013-2357-2

AUTORES / AUTHORS: - Rau BM
INSTITUCIÓN / INSTITUTION: - Department of General, Thoracic, Vascular, and Transplantation Surgery, University of Rostock, Schillingallee 35, 18057, Rostock, Germany, bettina.rau@med.uni-rostock.de.

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[18]
TÍTULO / TITLE: - Unexpected gain of function for the scaffolding protein plectin due to mislocalization in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Nov 26;110(48):19414-9. doi: 10.1073/pnas.1309720110. Epub 2013 Nov 11.
●● Enlace al texto completo (gratuito o de pago) 1073/pnas.1309720110
AUTORES / AUTHORS: - Shin SJ; Smith JA; Rezniczek GA; Pan S; Chen R; Brentnall TA; Wiche G; Kelly KA
INSTITUCIÓN / INSTITUTION: - Department of Biomedical Engineering, University of Virginia School of Engineering and Applied Sciences, Charlottesville, VA 22908.
RESUMEN / SUMMARY: - We recently demonstrated that plectin is a robust biomarker for pancreatic ductal adenocarcinoma (PDAC), one of the most aggressive malignancies. In normal physiology, plectin is an intracellular scaffolding protein, but we have demonstrated localization on the extracellular surface of PDAC cells. In this study, we confirmed cell surface localization. Interestingly, we found that plectin cell surface localization was attributable to its presence in exosomes secreted from PDAC cells, which is dependent on the expression of integrin beta4, a protein known to interact with cytosolic plectin. Moreover, plectin expression was necessary for efficient exosome production and was required to sustain enhanced tumor growth in immunodeficient and in immunocompetent mice. It is now clear that this PDAC biomarker plays a role in PDAC, and further understanding of plectin's contribution to PDAC could enable improved therapies.

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[19]
TÍTULO / TITLE: - Isoprenylcysteine carboxylmethyltransferase deficiency exacerbates KRAS-driven pancreatic neoplasia via Notch suppression.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Clin Invest. 2013 Oct 8. pii: 65764. doi: 10.1172/JCI65764.
●● Enlace al texto completo (gratuito o de pago) 1172/JCI65764
AUTORES / AUTHORS: - Court H; Amoyel M; Hackman M; Lee KE; Xu R; Miller G; Bar-Sagi D; Bach EA; Bergo MO; Philips MR
RESUMEN / SUMMARY: - RAS is the most frequently mutated oncogene in human cancers. Despite decades of effort, anti-RAS therapies have remained elusive. Isoprenylcysteine carboxylmethyltransferase (ICMT) methylates RAS and other CaaX-containing proteins, but its potential as a target for cancer therapy has not been fully evaluated. We crossed a Pdx1-Cre;LSL-KrasG12D mouse, which is a model of pancreatic ductal adenocarcinoma (PDA), with a mouse harboring a floxed allele of Icmt. Surprisingly, we found that ICMT deficiency dramatically accelerated the development and progression of neoplasia. ICMT-deficient pancreatic ductal epithelial cells had a slight growth advantage and were resistant to premature senescence by a

mechanism that involved suppression of cyclin-dependent kinase inhibitor 2A (p16INK4A) expression. ICMT deficiency precisely phenocopied Notch1 deficiency in the Pdx1-Cre;LSL-KrasG12D model by exacerbating pancreatic intraepithelial neoplasias, promoting facial papillomas, and derepressing Wnt signaling. Silencing ICMT in human osteosarcoma cells decreased Notch1 signaling in response to stimulation with cell-surface ligands. Additionally, targeted silencing of Ste14, the Drosophila homolog of Icmt, resulted in defects in wing development, consistent with Notch loss of function. Our data suggest that ICMT behaves like a tumor suppressor in PDA because it is required for Notch1 signaling.

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[20]

TÍTULO / TITLE: - MicroRNAs Cooperatively Inhibit a Network of Tumor Suppressor Genes to Promote Pancreatic Tumor Growth and Progression.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Oct 9. pii: S0016-5085(13)01431-5. doi: 10.1053/j.gastro.2013.10.010.

●● Enlace al texto completo (gratuito o de pago) 1053/j.gastro.2013.10.010

AUTORES / AUTHORS: - Frampton AE; Castellano L; Colombo T; Giovannetti E; Krell J; Jacob J; Pellegrino L; Roca-Alonso L; Funel N; Gall TM; De Giorgio A; Pinho FG; Fulci V; Britton DJ; Ahmad R; Habib NA; Coombes RC; Harding V; Knosel T; Stebbing J; Jiao LR

INSTITUCIÓN / INSTITUTION: - HPB Surgical Unit, Department of Surgery and Cancer, Imperial College, London, UK.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: There has not been a broad analysis of the combined effects of altered activities of microRNAs (miRNAs) in pancreatic ductal adenocarcinoma (PDAC) cells, and it is unclear how these might affect tumor progression or patient outcomes. METHODS: We combined data from miRNA and messenger RNA (mRNA) expression profiles and bioinformatic analyses to identify an miRNA-mRNA regulatory network in PDAC cell lines (PANC-1 and MIA PaCa-2) and in PDAC samples from patients. We used this information to identify miRNAs that contribute most to tumorigenesis. RESULTS: We identified 3 miRNAs (MIR21, MIR23A, and MIR27A) that acted as cooperative repressors of a network of tumor suppressor genes that included PDCD4, BTG2, and NEDD4L. Inhibition of MIR21, MIR23A, and MIR27A had synergistic effects in reducing proliferation of PDAC cells in culture and growth of xenograft tumors in mice. The level of inhibition was greater than that of inhibition of MIR21 alone. In 91 PDAC samples from patients, high levels of a combination of MIR21, MIR23A, and MIR27A were associated with shorter survival times after surgical resection. CONCLUSIONS: In an integrated data analysis, we identified functional miRNA-mRNA interactions that contribute to growth of PDACs. These findings indicate that miRNAs act together to promote tumor progression; therapeutic strategies might require inhibition of several miRNAs.

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[21]

TÍTULO / TITLE: - Loss of PTEN Expression Is Associated with Poor Prognosis in Patients with Intraductal Papillary Mucinous Neoplasms of the Pancreas.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 12.

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-0624

AUTORES / AUTHORS: - Garcia-Carracedo D; Turk AT; Fine SA; Akhavan N; Tweel BC; Parsons R; Chabot JA; Allendorf JD; Genkinger JM; Remotti HE; Su GH

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Herbert Irving Comprehensive Cancer Center; Departments of Pathology, Surgery, and Otolaryngology/Head and Neck Surgery; Institute for Cancer Genetics, Columbia University Medical Center; and The Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, New York.

RESUMEN / SUMMARY: - PURPOSE: Previously, we reported PIK3CA gene mutations in high-grade intraductal papillary mucinous neoplasms (IPMN). However, the contribution of phosphatidylinositol-3 kinase pathway (PI3K) dysregulation to pancreatic carcinogenesis is not fully understood and its prognostic value unknown. We investigated the dysregulation of the PI3K signaling pathway in IPMN and its clinical implication.EXPERIMENTAL DESIGN: Thirty-six IPMN specimens were examined by novel mutant-enriched sequencing methods for hot-spot mutations in the PIK3CA and AKT1 genes. PIK3CA and AKT1 gene amplifications and loss of heterozygosity at the PTEN locus were also evaluated. In addition, the expression levels of PDPK1/PDK1, PTEN, and Ki67 were analyzed by immunohistochemistry.RESULTS: Three cases carrying the E17K mutation in the AKT1 gene and one case harboring the H1047R mutation in the PIK3CA gene were detected among the 36 cases. PDK1 was significantly overexpressed in the high-grade IPMN versus low-grade IPMN (P = 0.034) and in pancreatic and intestinal-type of IPMN versus gastric-type of IPMN (P = 0.020). Loss of PTEN expression was strongly associated with presence of invasive carcinoma and poor survival in these IPMN patients (P = 0.014).CONCLUSION: This is the first report of AKT1 mutations in IPMN. Our data indicate that oncogenic activation of the PI3K pathway can contribute to the progression of IPMN, in particular loss of PTEN expression. This finding suggests the potential employment of PI3K pathway-targeted therapies for IPMN patients. The incorporation of PTEN expression status in making surgical decisions may also benefit IPMN patients and should warrant further investigation. Clin Cancer Res; 1-12. ©2013 AACR.

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[22]

TÍTULO / TITLE: - First Reported Case of Intentional Use of a Duodenal Stent to Treat Gastric Outlet Obstruction Prior to Pancreaticoduodenectomy in a Patient with Pancreatic Cancer.

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

REVISTA / JOURNAL: - Dig Dis Sci. 2013 Oct 11.

●● Enlace al texto completo (gratuito o de pago) 1007/s10620-013-2895-3

AUTORES / AUTHORS: - Ahmad S; Adler DG

INSTITUCIÓN / INSTITUTION: - Gastroenterology and Hepatology, Huntsman Cancer Center, University of Utah School of Medicine, 30N 1900E 4R118, Salt Lake City, UT, 84312, USA.

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[23]
TÍTULO / TITLE: - Pancreas cancer on the rise: are we up to the challenge?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Natl Cancer Inst. 2013 Nov 20;105(22):1675-6. doi: 10.1093/jnci/djt316. Epub 2013 Nov 7.
●● Enlace al texto completo (gratuito o de pago) 1093/jnci/djt316
AUTORES / AUTHORS: - Cardin DB; Berlin JD
INSTITUCIÓN / INSTITUTION: - Affiliation of authors: Department of Medicine, Vanderbilt University, Nashville, TN.

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[24]
TÍTULO / TITLE: - Loss of membranous expression of the intracellular domain of EpCAM is a frequent event and predicts poor survival in patients with pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Histopathology. 2013 Oct 9. doi: 10.1111/his.12307.
●● Enlace al texto completo (gratuito o de pago) 1111/his.12307
AUTORES / AUTHORS: - Fong D; Moser P; Kasal A; Seeber A; Gastl G; Martowicz A; Wurm M; Mian C; Obrist P; Mazzoleni G; Spizzo G
INSTITUCIÓN / INSTITUTION: - Tyrolean Cancer Research Institute, Laboratory for Experimental Oncology, Innsbruck, Austria; Department of Internal Medicine V, Hematology and Oncology, Medical University Innsbruck, Innsbruck, Austria; Department of Hematology and Oncology, Franz Tappeiner Hospital, Merano, Italy; Oncotyrol-Center for Personalized Cancer Medicine, Innsbruck, Austria.
RESUMEN / SUMMARY: - AIMS: Epithelial cell adhesion molecule (EpCAM) is a widely used immunohistochemical marker for epithelial human malignancies. Antibodies to target EpCAM are usually directed against its ectodomain (EpEX), but do not detect the intracellular domain (EpICD). The aim of this study was to compare membranous EpEX versus EpICD expression by immunohistochemistry. METHODS AND RESULTS: Concurrent EpEX and EpICD expression was investigated retrospectively in cancerous and matched non-neoplastic tissue samples from patients with pancreatic adenocarcinoma. In total, 317 paired samples of pancreatic tissue from 88 patients were analysed and correlated with clinicopathological parameters. In non-cancerous tissue, a high concordance of membranous EpEX and EpICD expression was observed and defined as the expression of the full-length EpCAM (EpEX+ /EpICD+ phenotype, EpCAMMF), which was highly predominant. In contrast, while most tumour samples were EpEX positive, loss of membranous EpICD expression (EpEX+ /EpICD- phenotype, EpCAMMT) was observed in one-third of cases, and these patients had a significantly shortened disease-free and overall survival. CONCLUSIONS: This study demonstrates for the first time that loss of membranous EpICD expression is a frequent event and predicts poor prognosis in patients with pancreatic cancer. Additional studies evaluating the predictive and prognostic value of the expression of different membranous EpCAM variants are warranted in epithelial cancers.

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[25]

TÍTULO / TITLE: - Prognostic and Predictive Blood-Based Biomarkers in Patients with Advanced Pancreatic Cancer: Results from CALGB80303 (Alliance).
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 12.
●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-0926
AUTORES / AUTHORS: - Nixon AB; Pang H; Starr MD; Friedman PN; Bertagnolli MM; Kindler HL; Goldberg RM; Venook AP; Hurwitz HI
INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Division of Medical Oncology; Alliance Statistics and Data Center, Duke University Medical Center; Durham, North Carolina; Section of Hematology/Oncology, University of Chicago Cancer Research Center; Chicago, Illinois; Department of Surgery, Brigham and Women's Hospital & Harvard Medical School; Boston, Massachusetts; Department of Internal Medicine, Ohio State University; Columbus, Ohio; and Division of Medical Oncology, University of California, San Francisco, California.
RESUMEN / SUMMARY: - PURPOSE: CALGB80303 was a phase III trial of 602 patients with locally advanced or metastatic pancreatic cancer comparing gemcitabine/bevacizumab versus gemcitabine/placebo. The study found no benefit in any outcome from the addition of bevacizumab to gemcitabine. Blood samples were collected and multiple angiogenic factors were evaluated and then correlated with clinical outcome in general (prognostic markers) and with benefit specifically from bevacizumab treatment (predictive markers).EXPERIMENTAL DESIGN: Plasma samples were analyzed via a novel multiplex ELISA platform for 31 factors related to tumor growth, angiogenesis, and inflammation. Baseline values for these factors were correlated with overall survival (OS) using univariate Cox proportional hazard regression models and multivariable Cox regression models with leave-one-out cross validation. Predictive markers were identified using a treatment by marker interaction term in the Cox model.RESULTS: Baseline plasma was available from 328 patients. Univariate prognostic markers for OS were identified including: Ang2, CRP, ICAM-1, IGFBP-1, TSP-2 (all $P < 0.001$). These prognostic factors were found to be highly significant, even after adjustment for known clinical factors. Additional modeling approaches yielded prognostic signatures from multivariable Cox regression. The gemcitabine/bevacizumab signature consisted of IGFBP-1, interleukin-6, PDGF-AA, PDGF-BB, TSP-2; whereas the gemcitabine/placebo signature consisted of CRP, IGFBP-1, PAI-1, PDGF-AA, P-selectin (both $P < 0.0001$). Finally, three potential predictive markers of bevacizumab efficacy were identified: VEGF-D ($P < 0.01$), SDF1 ($P < 0.05$), and Ang2 ($P < 0.05$).CONCLUSION: This study identified strong prognostic markers for pancreatic cancer patients. Predictive marker analysis indicated that plasma levels of VEGF-D, Ang2, and SDF1 significantly predicted for benefit or lack of benefit from bevacizumab in this population. Clin Cancer Res; 1-10. ©2013 AACR.

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[26]
TÍTULO / TITLE: - Anterior Gradient 2 and Mucin 4 Expression Mirrors Tumor Cell Differentiation in Pancreatic Adenocarcinomas, But Aberrant Anterior Gradient 2 Expression Predicts Worse Patient Outcome in Poorly Differentiated Tumors.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreas. 2013 Oct 30.

●● Enlace al texto completo (gratuito o de pago)
1097/MPA.0b013e3182a63bc3
AUTORES / AUTHORS: - Brychtova V; Hermanova M; Karasek P; Lenz J; Selingerova I; Vojtesek B; Kala Z; Hrstka R
INSTITUCIÓN / INSTITUTION: - From the *Regional Centre for Applied Molecular Oncology, Masaryk Memorial Cancer Institute; daggerFirst Department of Pathological Anatomy, St Anne's University Hospital, Medical Faculty of Masaryk University; double daggerDepartment of Complex Oncology Care, Masaryk Memorial Cancer Institute; section signDepartment of Mathematics and Statistics, Faculty of Science, Masaryk University; and parallelDepartment of Surgery, University Hospital Brno, Medical Faculty of Masaryk University, Brno, Czech Republic.
RESUMEN / SUMMARY: - OBJECTIVES: This study aimed to determine anterior gradient 2 (AGR2) expression in biopsies from pancreatic ductal adenocarcinomas (PDACs) and to evaluate AGR2 as a potential independent prognostic factor. METHODS: Tissue sample sections from a cohort of 135 consecutive surgically resectable PDACs were subjected to semiquantitative immunohistochemical analysis of AGR2 and mucin 4 (MUC4) expression. RESULTS: Anterior gradient 2 was over-expressed in PDAC compared with normal ductal cells. Since tumor lesions of PDAC are heterogeneous and constitute structures with various differentiation states, expression of both AGR2 and MUC4 was evaluated in each separate component. Expression levels of both proteins reflected the degree of tumor differentiation. Generally, well differentiated regions of tumor lesions expressed high levels of both proteins, moderately differentiated regions showed less AGR2 and MUC4, and poorly differentiated structures showed only weak positivity or were entirely negative. Of particular interest were occasional cases of strong AGR2 expression in high-grade tumors, where elevated protein levels were associated with shorter patient survival. CONCLUSIONS: Anterior gradient 2 and MUC4 reflect the level of differentiation of PDACs. However, in less differentiated tumors, aberrantly elevated AGR2 expression predicts poor patient outcome.

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[27]
TÍTULO / TITLE: - Development of a Mucin4-Targeting SPIO Contrast Agent for Effective Detection of Pancreatic Tumor Cells in Vitro and in Vivo.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Med Chem. 2013 Nov 27;56(22):9100-9. doi: 10.1021/jm401060z. Epub 2013 Nov 7.
●● Enlace al texto completo (gratuito o de pago) 1021/jm401060z
AUTORES / AUTHORS: - Wu SC; Chen YJ; Lin YJ; Wu TH; Wang YM
INSTITUCIÓN / INSTITUTION: - Department of Biological Science and Technology, Institute of Molecular Medicine and Bioengineering, National Chiao Tung University , 75 Bo-Ai Street, Hsinchu 300, Taiwan.
RESUMEN / SUMMARY: - In search of a unique and reliable contrast agent targeting pancreatic adenocarcinoma, new multifunctional nanoparticles (MnMEIO-silane-NH2-(MUC4)-mPEG NPs) were successfully developed in this study. Mucin4-expression levels were determined through different imaging studies in a panel of pancreatic tumor cells (HPAC, BxPC-3, and Panc-1) both in vitro and in vivo studies. The in vitro T2-weighted MR imaging study in HPAC and Panc-1 tumor cells treated with NPs showed

-89.1 +/- 5.7% and -0.9 +/- 0.2% contrast enhancement, whereas in in vivo study, it is found to be -81.5 +/- 4.5% versus -19.6 +/- 5.2% (24 h postinjection, 7.0 T), respectively. The T2-weighted MR and optical imaging studies revealed that the novel contrast agent can specifically and effectively target to mucin4-expressing tumors in nude mice. Hence, it is suggested that MnMEIO-silane-NH2-(MUC4)-mPEG NPs are able to provide an efficient and targeted delivery of MUC4 antibodies to mucin4-expressing pancreatic tumors.

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[28]

TÍTULO / TITLE: - Hepatobiliary and pancreatic neoplasms in patients with McCune-Albright syndrome.

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

REVISTA / JOURNAL: - J Clin Endocrinol Metab. 2013 Oct 29.

●● Enlace al texto completo (gratuito o de pago) 1210/jc.2013-1823

AUTORES / AUTHORS: - Gaujoux S; Salenave S; Ronot M; Rangheard AS; Cros J; Belghiti J; Sauvanet A; Ruszniewski P; Chanson P

INSTITUCIÓN / INSTITUTION: - 1 AP-HP, Hopital Beaujon, Department of Hepato-Pancreato-Biliary Surgery - Pole des Maladies de l'Appareil Digestif (PClichy, 92110, France;

RESUMEN / SUMMARY: - Background:McCune-Albright syndrome, which includes polycystic fibrous dysplasia, precocious puberty, and cafe au lait spots, is a rare disorder caused by somatic activating mutations of the GNAS gene. GNAS mutations have also been implicated in various sporadic tumors, including hepatobiliary and pancreatic neoplasms.Aim of the study:The aim of this study was to assess the prevalence of hepatobiliary and pancreatic neoplasms in patients McCune-Albright syndrome.Patients and methods:Nineteen patients diagnosed between 1995 and 2012 with MAS in a tertiary referal center for rare growth disorders were screened with dedicated gadolinium-enhanced magnetic resonance imaging for hepatobiliary and pancreatic neoplasms between June 2011 and December 2012.Results:Six (32%) of the 19 screened patients were found to have hepatic, pancreatic or biliary lesions, excluding liver hemangiomas, liver cysts and focal nodular hyperplasia. This includes pancreatic ductal lesions observed in 4 patients, including numerous branch-duct IPMN in 3 patients. Biliary lesions were observed in one patient, with a large choledocal cyst also involving the left biliary branch. Finally, multiple inflammatory/telangiectatic hepatic adenomas were observed in two patients, including one with proven somatic GNAS mutation.Conclusion:We herein describe the first observation of syndromic IPMN and a the new association between McCune-Albright syndrome and pancreatic neoplasms, namely intraductal papillary mucinous neoplasms of the pancreas but also rare hepatobiliary neoplasms including liver adenomas and choledochal cysts. These findings strongly suggest somatic activating GNAS mutations possibly trough cAMP pathway disorders to be involved in the tumorigenesis of hepatobiliary and pancreatic tissues originating from the foregut endoderm, and have lead us to use a routine screening by dedicated MRI including both pancreatobiliary and liver sequences in patients with MAS.

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[29]

TÍTULO / TITLE: - Effects of intercellular junction protein expression on intracellular ice formation in mouse insulinoma cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Biophys J. 2013 Nov 5;105(9):2006-15. doi: 10.1016/j.bpj.2013.09.028.
●● Enlace al texto completo (gratuito o de pago) 1016/j.bpj.2013.09.028
AUTORES / AUTHORS: - Higgins AZ; Karlsson JO
INSTITUCIÓN / INSTITUTION: - School of Chemical, Biological and Environmental Engineering, Oregon State University, Corvallis, Oregon.
RESUMEN / SUMMARY: - The development of cryopreservation procedures for tissues has proven to be difficult in part because cells within tissue are more susceptible to intracellular ice formation (IIF) than are isolated cells. In particular, previous studies suggest that cell-cell interactions increase the likelihood of IIF by enabling propagation of ice between neighboring cells, a process thought to be mediated by gap junction channels. In this study, we investigated the effects of cell-cell interactions on IIF using three genetically modified strains of the mouse insulinoma cell line MIN6, each of which expressed key intercellular junction proteins (connexin-36, E-cadherin, and occludin) at different levels. High-speed video cryomicroscopy was used to visualize the freezing process in pairs of adherent cells, revealing that the initial IIF event in a given cell pair was correlated with a hitherto unrecognized precursor phenomenon: penetration of extracellular ice into paracellular spaces at the cell-cell interface. Such paracellular ice penetration occurred in the majority of cell pairs observed, and typically preceded and colocalized with the IIF initiation events. Paracellular ice penetration was generally not observed at temperatures >-5.65 degrees C, which is consistent with a penetration mechanism via defects in tight-junction barriers at the cell-cell interface. Although the maximum temperature of paracellular penetration was similar for all four cell strains, genetically modified cells exhibited a significantly higher frequency of ice penetration and a higher mean IIF temperature than did wild-type cells. A four-state Markov chain model was used to quantify the rate constants of the paracellular ice penetration process, the penetration-associated IIF initiation process, and the intercellular ice propagation process. In the initial stages of freezing (>-15 degrees C), junction protein expression appeared to only have a modest effect on the kinetics of propagative IIF, and even cell strains lacking the gap junction protein connexin-36 exhibited nonnegligible ice propagation rates.

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[30]
TÍTULO / TITLE: - Targeting CXCL12 from FAP-expressing carcinoma-associated fibroblasts synergizes with anti-PD-L1 immunotherapy in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Nov 25.
●● Enlace al texto completo (gratuito o de pago) 1073/pnas.1320318110
AUTORES / AUTHORS: - Feig C; Jones JO; Kraman M; Wells RJ; Deonarine A; Chan DS; Connell CM; Roberts EW; Zhao Q; Caballero OL; Teichmann SA; Janowitz T; Jodrell DI; Tuveson DA; Fearon DT
INSTITUCIÓN / INSTITUTION: - Cancer Research UK Cambridge Institute, Li Ka Shing Centre, University of Cambridge, Cambridge CB2 0RE, United Kingdom.

RESUMEN / SUMMARY: - An autochthonous model of pancreatic ductal adenocarcinoma (PDA) permitted the analysis of why immunotherapy is ineffective in this human disease. Despite finding that PDA-bearing mice had cancer cell-specific CD8+ T cells, the mice, like human patients with PDA, did not respond to two immunological checkpoint antagonists that promote the function of T cells: anti-cytotoxic T-lymphocyte-associated protein 4 (alpha-CTLA-4) and alpha-programmed cell death 1 ligand 1 (alpha-PD-L1). Immune control of PDA growth was achieved, however, by depleting carcinoma-associated fibroblasts (CAFs) that express fibroblast activation protein (FAP). The depletion of the FAP+ stromal cell also uncovered the antitumor effects of alpha-CTLA-4 and alpha-PD-L1, indicating that its immune suppressive activity accounts for the failure of these T-cell checkpoint antagonists. Three findings suggested that chemokine (C-X-C motif) ligand 12 (CXCL12) explained the overriding immunosuppression by the FAP+ cell: T cells were absent from regions of the tumor containing cancer cells, cancer cells were coated with the chemokine, CXCL12, and the FAP+ CAF was the principal source of CXCL12 in the tumor. Administering AMD3100, a CXCL12 receptor chemokine (C-X-C motif) receptor 4 inhibitor, induced rapid T-cell accumulation among cancer cells and acted synergistically with alpha-PD-L1 to greatly diminish cancer cells, which were identified by their loss of heterozygosity of Trp53 gene. The residual tumor was composed only of premalignant epithelial cells and inflammatory cells. Thus, a single protein, CXCL12, from a single stromal cell type, the FAP+ CAF, may direct tumor immune evasion in a model of human PDA.

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[31]

TÍTULO / TITLE: - Pancreatic intraepithelial neoplasia and histological changes in non-neoplastic pancreas associated with neoadjuvant therapy in patients with pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Histopathology. 2013 Dec;63(6):841-51. doi: 10.1111/his.12234. Epub 2013 Sep 20.

●● Enlace al texto completo (gratuito o de pago) 1111/his.12234

AUTORES / AUTHORS: - Chatterjee D; Katz MH; Rashid A; Estrella JS; Wang H; Varadhachary GR; Wolff RA; Lee JE; Pisters PW; Abbruzzese JL; Fleming JB; Wang H

INSTITUCIÓN / INSTITUTION: - Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA.

RESUMEN / SUMMARY: - AIMS: To study the histological changes in non-neoplastic pancreas and the effects on pancreatic intraepithelial neoplasia (PanIN) after neoadjuvant chemoradiation therapy (NCRT) for pancreatic ductal adenocarcinoma (PDAC). METHODS AND RESULTS: We reviewed the archival H&E slides from 218 patients with PDAC who completed NCRT and pancreaticoduodenectomy. Sixty-five patients who underwent pancreaticoduodenectomy for PDAC without NCRT were used as controls. Various histological features were reviewed and correlated with NCRT and survival. The NCRT group had lower densities of PanIN2 ($P = 0.004$) and PanIN3 ($P = 0.02$) than the control group. The extent of fibrosis, the frequency of neuroma-like nerve proliferation and the frequency of islet cell aggregation were significantly higher in the NCRT group than in the control group ($P < 0.05$). The intensity of inflammation was less in the NCRT group than in the control group ($P = 0.02$). In the NCRT group,

patents with moderate to severe fibrosis or grade 2 inflammation had poorer survival than those with mild fibrosis (P = 0.04) or those with grade 0 or grade 1 inflammation (P = 0.003), respectively. CONCLUSIONS: Non-neoplastic pancreatic tissue from patients who received NCRT had a reduced density of high-grade PanIN lesions, more pancreatic fibrosis, and higher frequencies of neuroma-like nerve proliferation and islet cell aggregation, but less inflammation, compared to tissue from those who did not receive NCRT.

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[32]

TÍTULO / TITLE: - Adjuvant chemotherapy in elderly patients with pancreatic cancer.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 21. doi: 10.1038/bjc.2013.722.

●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.722

AUTORES / AUTHORS: - Nagrial AM; Chang DK; Nguyen NQ; Johns AL; Chantrill LA; Humphris JL; Chin VT; Samra JS; Gill AJ; Pajic M; Pinese M; Colvin EK; Scarlett CJ; Chou A; Kench JG; Sutherland RL; Horvath LG; Biankin AV

INSTITUCIÓN / INSTITUTION: - The Kinghorn Cancer Centre, and the Cancer Research Program, Garvan Institute of Medical Research, 384 Victoria Street, Darlinghurst, Sydney NSW 2010, Australia.

RESUMEN / SUMMARY: - Background:Adjuvant chemotherapy improves survival for patients with resected pancreatic cancer. Elderly patients are under-represented in Phase III clinical trials, and as a consequence the efficacy of adjuvant therapy in older patients with pancreatic cancer is not clear. We aimed to assess the use and efficacy of adjuvant chemotherapy in older patients with pancreatic cancer.Methods:We assessed a community cohort of 439 patients with a diagnosis of pancreatic ductal adenocarcinoma who underwent operative resection in centres associated with the Australian Pancreatic Cancer Genome Initiative.Results:The median age of the cohort was 67 years. Overall only 47% of all patients received adjuvant therapy. Patients who received adjuvant chemotherapy were predominantly younger, had later stage disease, more lymph node involvement and more evidence of perineural invasion than the group that did not receive adjuvant treatment. Overall, adjuvant chemotherapy was associated with prolonged survival (median 22.1 vs 15.8 months; P<0.0001). Older patients (aged >/=70) were less likely to receive adjuvant chemotherapy (51.5% vs 29.8%; P<0.0001). Older patients had a particularly poor outcome when adjuvant therapy was not delivered (median survival=13.1 months; HR 1.89, 95% CI: 1.27-2.78, P=0.002).Conclusion:Patients aged >/=70 are less likely to receive adjuvant therapy although it is associated with improved outcome. Increased use of adjuvant therapy in older individuals is encouraged as they constitute a large proportion of patients with pancreatic cancer.British Journal of Cancer advance online publication, 21 November 2013; doi:10.1038/bjc.2013.722 www.bjcancer.com.

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[33]

TÍTULO / TITLE: - The ATP-Competitive mTOR Inhibitor INK128 enhances in vitro and in vivo radiosensitivity of pancreatic carcinoma cells.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 6.

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-2136

AUTORES / AUTHORS: - Hayman TJ; Wahba A; Rath BH; Bae H; Kramp T; Shankavaram U; Camphausen KA; Tofilon PJ

INSTITUCIÓN / INSTITUTION: - Morsani College of Medicine, University of South Florida.

RESUMEN / SUMMARY: - PURPOSE: Radiotherapy remains a primary treatment modality for pancreatic carcinoma, a tumor characterized by aberrant mTOR activity. Given mTOR's regulatory role in gene translation, in this study we defined the effects of the clinically relevant, ATP-competitive mTOR inhibitor, INK128 on the radiosensitivity of pancreatic carcinoma cell lines. EXPERIMENTAL DESIGN: Clonogenic survival was used to determine the effects of INK128 on in vitro radiosensitivity on 3 pancreatic carcinoma cell lines and a normal fibroblast cell line with mTOR activity defined using immunoblots. DNA double strand breaks were evaluated according to gammaH2AX foci. The influence of INK128 on radiation-induced gene translation was determined by microarray analysis of polysome-bound mRNA. Leg tumor xenografts grown from pancreatic carcinoma cells were evaluated for mTOR activity, eIF4F cap complex formation and tumor growth delay. RESULTS: INK128, while inhibiting mTOR activity in each of the cell lines, enhanced the in vitro radiosensitivity of the pancreatic carcinoma cells, but had no effect on normal fibroblasts. The dispersal of radiation-induced gammaH2AX foci was inhibited in pancreatic carcinoma cells by INK128 as were radiation-induced changes in gene translation. Treatment of mice with INK128 resulted in an inhibition of mTOR activity as well as cap-complex formation in tumor xenografts. Whereas INK128 alone had no effect of tumor growth rate, it enhanced the tumor growth delay induced by single and fractionated doses of radiation. CONCLUSIONS: These results indicate that mTOR inhibition induced by INK128 enhances the radiosensitivity of pancreatic carcinoma cells and suggest that this effect involves the inhibition of DNA repair.

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[34]

TÍTULO / TITLE: - Efficacy of nimotuzumab plus gemcitabine usage as first-line treatment in patients with advanced pancreatic cancer.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 19.

●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-1306-x

AUTORES / AUTHORS: - Su D; Jiao SC; Wang LJ; Shi WW; Long YY; Li J; Bai L

INSTITUCIÓN / INSTITUTION: - Department of Oncology Medicine, Chinese PLA General Hospital, No. 28 Fuxing Road, Haidian District, Beijing, 100853, China.

RESUMEN / SUMMARY: - Advanced pancreatic cancer patients have poor prognosis and scarcely respond to conventional therapies. Clinical trials support the use of molecular-targeted therapy against epidermal growth factor receptor (EGFR) signaling. The objective of the current study was to evaluate the contribution of a monoclonal antibody against EGFR, nimotuzumab, to standard gemcitabine therapy. Patients with unresectable locally advanced or metastatic pancreatic adenocarcinoma were assigned to receive gemcitabine plus nimotuzumab. The primary end point was overall survival, whereas the secondary end points included progression-free survival, objective response, and adverse side effects. A total of 18 eligible patients were

accrued between December 2007 and July 2010. The disease control rate, calculated as the sum of complete response, partial response, and stable disease, was 55.6 %. The median overall survival time was 9.29 months (95 % CI, 5.499 to 13.072). The median progression-free survival was 3.71 months (95 % CI, 2.526 to 4.902), and the 1-year survival rate was 38.9 %. Of all the patients, 88.8 % had at least one adverse side effect; however, no grade 4 adverse side effect was reported. Nimotuzumab as a high-purity humanized monoclonal antibody with favorable safety profile, its value in the treatment of pancreatic cancer along with gemcitabine, particularly in the comprehensive treatment of advanced pancreatic cancer, is appealing for further prospective randomized large-scale clinical trials.

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[35]

TÍTULO / TITLE: - Phase II clinical study of alternate-day oral therapy with S-1 as first-line chemotherapy for locally advanced and metastatic pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Oct 22.

●● Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2323-6

AUTORES / AUTHORS: - Yamaue H; Satoi S; Kanbe T; Miyazawa M; Tani M; Kawai M; Hirono S; Okada K; Yanagimoto H; Kwon AH; Mukouyama T; Tsunoda H; Chijiiwa K; Ohuchida J; Kato J; Ueda K; Yamaguchi T; Egawa S; Hayashi K; Shirasaka T

INSTITUCIÓN / INSTITUTION: - Second Department of Surgery, Wakayama Medical University, 10-31 Kimiidera, Wakayama City, Wakayama, 641-8510, Japan, yamaue-h@wakayama-med.ac.jp.

RESUMEN / SUMMARY: - PURPOSE: Based on the results of first-line chemotherapy for advanced pancreatic cancer, S-1 was confirmed to be non-inferior to gemcitabine. However, the recommended regimen of 4 weeks of administration followed by 2 weeks of drug withdrawal frequently causes adverse effects. On the other hand, we experienced in clinical practice that alternate-day administration of S-1 reduced adverse effects and were tolerable for advanced pancreatic cancer patients unwilling to continue the standard daily administration. We therefore conducted a multicenter cooperative prospective study to compare daily with alternate-day administration of S-1 for advanced pancreatic cancer. METHODS: Patients with advanced pancreatic cancer were eligible for enrollment in this trial. S-1 was administered at a dose of 40-60 mg twice daily, calculated according to body surface area, on Monday, Wednesday, Friday, and Sunday. Each treatment cycle was 42 days. The primary end point was overall survival (OS). Secondary end points were safety, response rate (RR), progression-free survival (PFS), and time to treatment failure (TTF). RESULTS: Forty-eight patients were evaluable for response. OS as the primary end point was 8.4 months (95 % CI 5.4-10.8), and the 1-year survival rate was 29.2 %. PFS was 5.5 months, and TTF was 3.9 months. RR was 10.4 %, and the disease control rate was 79.2 %. Grade ¾ hematological and non-hematological toxicities were minor. All of these adverse reactions were tolerable and reversible. CONCLUSIONS: The current data demonstrate the mitigation of adverse effects with alternate-day administration of S-1, and this appears to be a more sustainable option for advanced pancreatic cancer.

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[36]

TÍTULO / TITLE: - Commonality and differences of methylation signatures in the plasma of patients with pancreatic cancer and colorectal cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Int J Cancer. 2013 Nov 8. doi: 10.1002/ijc.28593.
●● Enlace al texto completo (gratuito o de pago) 1002/ijc.28593
AUTORES / AUTHORS: - Melson J; Li Y; Cassinotti E; Melnikov A; Boni L; Ai J; Greenspan M; Mobarhan S; Levenson V; Deng Y
INSTITUCIÓN / INSTITUTION: - Division of Digestive Diseases, Rush University Medical Center, Chicago, IL.
RESUMEN / SUMMARY: - Profiling of DNA methylation status of specific genes is a way to screen for colorectal cancer (CRC) and pancreatic cancer (PC) in blood. The commonality of methylation status of cancer-related tumor suppressor genes between CRC and PC is largely unknown. Methylation status of 56 cancer-related genes was compared in plasma of patients in the following cohorts: CRC, PC and healthy controls. Cross validation determined the best model by area under ROC curve (AUC) to differentiate cancer methylation profiles from controls. Optimal preferential gene methylation signatures were derived to differentiate either cancer (CRC or PC) from controls. For CRC alone, a three gene signature (CYCD2, HIC and VHL) had an AUC 0.9310, sensitivity (Sens) = 0.826, specificity (Spec) = 0.9383. For PC alone, an optimal signature consisted of five genes (VHL, MYF3, TMS, GPC3 and SRBC), AUC 0.848; Sens = 0.807, Spec = 0.666. Combined PC and CRC signature or “combined cancer signature” was derived to differentiate either CRC and PC from controls (MDR1, SRBC, VHL, MUC2, RB1, SYK and GPC3) AUC = 0.8177, Sens = 0.6316 Spec = 0.840. In a validation cohort, N = 10 CRC patients, the optimal CRC signature (CYCD2, HIC and VHL) had AUC 0.900. In all derived signatures (CRC, PC and combined cancer signature) the optimal panel used preferential VHL methylation. In conclusion, CRC and PC differ in specific genes methylated in plasma other than VHL. Preferential methylation of VHL is shared in the optimal signature for CRC alone, PC alone and combined PC and CRC. Future investigations may identify additional methylation markers informative for the presence of both CRC and PC.

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[37]
TÍTULO / TITLE: - Prediagnostic body mass index and pancreatic cancer survival.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Clin Oncol. 2013 Nov 20;31(33):4229-34. doi: 10.1200/JCO.2013.51.7532. Epub 2013 Oct 21.
●● Enlace al texto completo (gratuito o de pago) 1200/JCO.2013.51.7532
AUTORES / AUTHORS: - Yuan C; Bao Y; Wu C; Kraft P; Ogino S; Ng K; Qian ZR; Rubinson DA; Stampfer MJ; Giovannucci EL; Wolpin BM
INSTITUCIÓN / INSTITUTION: - Chen Yuan, Shuji Ogino, Kimmie Ng, Zhi Rong Qian, Douglas A. Rubinson, and Brian M. Wolpin, Dana-Farber Cancer Institute; Ying Bao, Shuji Ogino, Kimmie Ng, Meir J. Stampfer, Edward L. Giovannucci, and Brian M. Wolpin, Brigham and Women’s Hospital, Harvard Medical School; and Chen Wu, Peter Kraft, Shuji Ogino, Meir J. Stampfer, and Edward L. Giovannucci, Harvard School of Public Health, Boston, MA.
RESUMEN / SUMMARY: - PURPOSE: Although obesity is associated with increased incidence of pancreatic cancer, studies have not prospectively evaluated prediagnostic

body mass index (BMI) and survival. PATIENTS AND METHODS: We analyzed survival by prediagnostic BMI assessed in 1986 among 902 patients from two large prospective cohorts diagnosed from 1988 to 2010. We estimated hazard ratios (HRs) for death using Cox proportional hazards models, with adjustment for age, sex, race/ethnicity, smoking, diagnosis year, and stage. We evaluated the temporal association of BMI with survival by grouping reported BMI by 2-year lag-time intervals before diagnosis. RESULTS: The multivariable-adjusted HR for death was 1.53 (95% CI, 1.11 to 2.09) comparing patients with BMI >/= 35 kg/m(2) with those with BMI < 25 kg/m(2) (P trend = .001), which was similar after adjustment for stage. The association of BMI with survival was stronger with longer lag times between reported BMI and cancer diagnosis. Among patients with BMI collected 18 to 20 years before diagnosis, HR for death was 2.31 (95% CI, 1.48 to 3.61; P trend < .001), comparing obese with healthy-weight patients. No statistically significant differences were seen by cohort, smoking status, or stage, although the association was stronger among never-smokers (HR, 1.61; 95% CI, 1.01 to 2.57; P trend = .002) than ever-smokers (HR, 1.36; 95% CI, 0.86 to 2.15; P trend = .63), comparing BMI >/= 35 kg/m(2) with BMI < 25 kg/m(2). Higher prediagnostic BMI was associated with more advanced stage at diagnosis, with 72.5% of obese patients presenting with metastatic disease versus 59.4% of healthy-weight patients (P = .02). CONCLUSION: Higher prediagnostic BMI was associated with statistically significantly decreased survival among patients with pancreatic cancer from two large prospective cohorts.

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[38]

TÍTULO / TITLE: - Analysis of germline gene copy number variants of patients with sporadic pancreatic adenocarcinoma reveals specific variations.

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

REVISTA / JOURNAL: - Oncology. 2013;85(5):306-11. doi: 10.1159/000354737. Epub 2013 Nov 9.

●● Enlace al texto completo (gratuito o de pago) 1159/000354737

AUTORES / AUTHORS: - Fanale D; Iovanna JL; Calvo EL; Berthezene P; Belleau P; Dagorn JC; Ancona C; Catania G; D'Alia P; Galvano A; Gulotta E; Lo Dico S; Passiglia F; Bronte G; Midiri M; Lo Re G; Cicero G; Bazan V; Russo A

INSTITUCIÓN / INSTITUTION: - Section of Medical Oncology, Department of Surgical, Oncological and Stomatological Sciences,University of Palermo, Palermo, Italy.

RESUMEN / SUMMARY: - Objectives: The rapid fatality of pancreatic cancer is, in large part, the result of diagnosis at an advanced stage in the majority of patients. Identification of individuals at risk of developing pancreatic adenocarcinoma would be useful to improve the prognosis of this disease. There is presently no biological or genetic indicator allowing the detection of patients at risk. Our main goal was to identify copy number variants (CNVs) common to all patients with sporadic pancreatic cancer. Methods: We analyzed gene CNVs in leukocyte DNA from 31 patients with sporadic pancreatic adenocarcinoma and from 93 matched controls. Genotyping was performed with the use of the GeneChip Human Mapping 500K Array Set (Affymetrix). Results: We identified 431 single nucleotide polymorphism (SNP) probes with abnormal hybridization signal present in the DNA of all 31 patients. Of these SNP probes, 284 corresponded to 3 or more copies and 147 corresponded to 1 or 0 copies. Several cancer-associated genes were amplified in all patients. Conversely, several genes

supposed to oppose cancer development were present as single copy. Conclusions: These data suggest that a set of 431 CNVs could be associated with the disease. This set could be useful for early diagnosis. © 2013 S. Karger AG, Basel.

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[39]
TÍTULO / TITLE: - Expression of microRNA-218 in human pancreatic ductal adenocarcinoma and its correlation with tumor progression and patient survival.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Surg Oncol. 2013 Oct 25. doi: 10.1002/jso.23475.
●● Enlace al texto completo (gratuito o de pago) 1002/jso.23475
AUTORES / AUTHORS: - Zhu Z; Xu Y; Du J; Tan J; Jiao H
INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, First Hospital Affiliated to the Chinese PLA General Hospital, Beijing, People's Republic of China.
RESUMEN / SUMMARY: - BACKGROUND: Our aim was to analyze clinicopathologic and prognostic values of microRNA (miR)-218 in pancreatic ductal adenocarcinima (PDAC). METHODS: TaqMan quantitative RT-PCR was used to determine the expression of miR-218 in human PDAC cells and tissue samples. The association of miR-218 expression with clinicopathologic variables was analyzed. Kaplan-Meier survival analysis was performed to analyze the association of miR-218 expression with recurrence-free survival or overall survival of patients. Univariate and multivariate Cox regression analyses were performed. RESULTS: The relative level of miR-218 in PDAC cells was significantly lower than that in normal human pancreatic duct epithelial cell line. Also, the mean level of miR-218 in PDAC tissues was significantly lower than that in normal pancreatic tissues. Statistical analyses indicated that low miR-218 expression was closely associated with poor tumor differentiation, advanced tumor stage, higher incidence of lymph node metastasis, and tumor recurrence. Kaplan-Meier survival analyses showed that patients with low miR-218 expression had lower recurrence-free and overall survival than those with high miR-218 expression. Univariate and multivariate Cox regression analyses showed that miR-218 might be an independent prognostic factor. CONCLUSION: Reduced miR-218 in PDAC tissues was correlated with tumor progression, and might be an independent poor prognostic factor for patients. J. Surg. Oncol. © 2013 Wiley Periodicals, Inc.

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[40]
TÍTULO / TITLE: - High Intensity Focused Ultrasound Treatment for Patients with Local Advanced Pancreatic Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Oct 2;60(128). doi: 10.5754/hge13498.
●● Enlace al texto completo (gratuito o de pago) 5754/hge13498
AUTORES / AUTHORS: - Gao HF; Wang K; Meng ZQ; Chen Z; Lin JH; Zhou ZH; Wang P; Shi WD; Sheng YH
RESUMEN / SUMMARY: - :Background/Aims: To evaluate the safety and efficacy of high intensity focused ultrasound (HIFU) therapy in patients with local advanced pancreatic cancer. Methodology: 39 patients with local advanced pancreatic cancer were treated with HIFU, including 26 male and 13 female patients. The locations of the

tumours were as follows: head of pancreas in 7 patients, body and/or tail of pancreas in 32 patients. Pain relief, time to progression (TTP), median survival and complications were analysed after HIFU treatment. Results: There were no severe complications or adverse events related to HIFU therapy in any of the patients treated. Pain relief was achieved in 79.5% of patients. Median TTP was 5.0 months. The median overall survival time was 11 months. 6-month and 1-year survival rate for patients were 82.1% and 30.8% respectively. Conclusions: Although this study may have limitations, preliminary results demonstrate the safety of clinical application of HIFU for pancreatic cancer and reveal it to be a promising mode of treatment for local advanced pancreatic cancers.

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[41]

TÍTULO / TITLE: - Ran GTPase protein promotes human pancreatic cancer proliferation by deregulating the expression of Survivin and cell cycle proteins.

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

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Oct 18;440(2):322-9. doi: 10.1016/j.bbrc.2013.09.079. Epub 2013 Sep 25.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bbrc.2013.09.079

AUTORES / AUTHORS: - Deng L; Lu Y; Zhao X; Sun Y; Shi Y; Fan H; Liu C; Zhou J; Nie Y; Wu K; Fan D; Guo X

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Cancer Biology, Xijing Hospital of Digestive Diseases, Fourth Military Medical University, Xi'an, Shaanxi 710032, China; Department of Oncology, Tangdu Hospital, Fourth Military Medical University, Xi'an, Shaanxi 710038, China.

RESUMEN / SUMMARY: - Ran, a member of the Ras GTPase family, has important roles in nucleocytoplasmic transport. Herein, we detected Ran expression in pancreatic cancer and explored its potential role on tumour progression. Overexpressed Ran in pancreatic cancer tissues was found highly correlated with the histological grade. Downregulation of Ran led to significant suppression of cell proliferation, cell cycle arrest at the G1/S phase and induction of apoptosis. In vivo studies also validated that result. Further studies revealed that those effects were at least partly mediated by the downregulation of Cyclin A, Cyclin D1, Cyclin E, CDK2, CDK4, phospho-Rb and Survivin proteins and up regulation of cleaved Caspase-3.

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[42]

TÍTULO / TITLE: - Smoking and Body Mass Index and Survival in Pancreatic Cancer Patients.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct 30.

●● Enlace al texto completo (gratuito o de pago)
1097/MPA.0b013e3182a7c74b

AUTORES / AUTHORS: - Pelucchi C; Galeone C; Polesel J; Manzari M; Zucchetto A; Talamini R; Franceschi S; Negri E; La Vecchia C

INSTITUCIÓN / INSTITUTION: - From the *Dipartimento di Epidemiologia, IRCCS-Istituto di Ricerche Farmacologiche Mario Negri; daggerDipartimento di Scienze Cliniche e di Comunita, Universita degli Studi di Milano, Milan; double daggerS.O.C. di

Epidemiologia e Biostatistica, IRCCS-Centro di Riferimento Oncologico, Aviano (PN); section signDipartimento di Traumatologia, Ortopedia e Medicina del Lavoro, Universita degli Studi di Torino, Turin, Italy; and parallelInternational Agency for Research on Cancer, Lyon, France.

RESUMEN / SUMMARY: - OBJECTIVE: The objective of this study was to provide further information on the role of personal characteristics and lifestyle factors, including obesity, diabetes, and tobacco smoking, on survival from pancreatic cancer. METHODS: We obtained follow-up data of pancreatic cancer patients enrolled in 2 Italian case-control studies. Information on characteristics and habits up to the time of diagnosis was collected by trained interviewers. Vital status was ascertained through population registers and record linkage with health system databases. Hazard ratios (HRs) of all-cause mortality and 95% confidence intervals (CIs) were estimated using Cox proportional hazards models. RESULTS: Follow-up information was retrieved for 648 cancer patients. Compared with subjects with body mass index of less than 25 kg/m, the HRs were 1.14 (95% CI, 0.94-1.39) for overweight (ie, 25-29.9 kg/m) and 1.32 (95% CI, 0.98-1.79) for obese (ie, >/=30 kg/m) patients (trend P = 0.046). The HRs were 1.37 (95% CI, 1.14-1.65) for ever, 1.30 (95% CI, 1.03-1.65) for ex-smokers, and 1.42 (95% CI, 1.16-1.73) for current versus never smokers. Increasing amount and duration of smoking were associated with reduced survival after pancreatic cancer. No association emerged with diabetes, alcohol consumption, and diet. CONCLUSIONS: Smoking and overweight before diagnosis may play a role in the prognosis of pancreatic cancer, besides its etiology.

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[43]

TÍTULO / TITLE: - Emetine enhances the tumor necrosis factor-related apoptosis-inducing ligand-induced apoptosis of pancreatic cancer cells by downregulation of myeloid cell leukemia sequence-1 protein.

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

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):456-62. doi: 10.3892/or.2013.2838. Epub 2013 Nov 7.

●● Enlace al texto completo (gratuito o de pago) 3892/or.2013.2838

AUTORES / AUTHORS: - Han Y; Park S; Kinyua AW; Andera L; Kim KW; Kim I

INSTITUCIÓN / INSTITUTION: - Asan Institute for Life Sciences, Asan Medical Center, Seoul 138-736, Republic of Korea.

RESUMEN / SUMMARY: - Although the tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) is a promising cancer therapeutic agent, it shows limited efficacy in human pancreatic cancer cells. Protein synthesis inhibition has been reported to sensitize cancer cells to apoptosis-inducing agents, but the detailed mechanism by which protein synthesis inhibition sensitize cells to TRAIL has not been determined. To investigate the mechanism underlying pancreatic cancer cell resistance to TRAIL, we performed a small scale high-throughput compound screening in AsPC-1 pancreatic cancer cells using a bioactive small molecule library. We identified 8 compounds that reproducibly sensitize AsPC-1 cells to TRAIL-induced apoptosis. One of these compounds, emetine hydrochloride, when combined with subtoxic concentrations of TRAIL, induced massive apoptosis in AsPC-1 and BxPC-3 pancreatic cancer cells. Cell death analysis revealed that the sensitizing effects of emetine were specific to TRAIL. Emetine downregulated the expression of the TRAIL-related anti-

apoptotic protein Mcl-1 in a dose- and time-dependent manner. Furthermore, specific knockdown of Mcl-1 using small interfering RNA without emetine treatment sensitized pancreatic cancer cells to TRAIL. Emetine sensitization of pancreatic cancer cells to TRAIL via Mcl-1 was confirmed under hypoxic conditions. Taken together, these findings strongly suggest that Mcl-1 is involved in pancreatic cancer cell resistance to TRAIL, and emetine facilitates the apoptosis of TRAIL-tolerant pancreatic cancer cells by specifically inhibiting Mcl-1 function.

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[44]

TÍTULO / TITLE: - Pancreatic stellate cells promote hapto-migration of cancer cells through collagen I-mediated signalling pathway.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 7. doi: 10.1038/bjc.2013.706.

●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.706

AUTORES / AUTHORS: - Lu J; Zhou S; Siech M; Habisch H; Seufferlein T; Bachem MG

INSTITUCIÓN / INSTITUTION: - Department of Clinical Chemistry, University of Ulm, Albert-Einstein-Allee 23, 89081, Ulm, Germany.

RESUMEN / SUMMARY: - Background:Pancreatic stellate cells (PSCs) promote metastasis as well as local growth of pancreatic cancer. However, the factors mediating the effect of PSCs on pancreatic cancer cells have not been clearly identified.Methods:We used a modified Boyden chamber assay as an in vitro model to investigate the role of PSCs in migration of Panc1 and UlaPaCa cells and to identify the underlying mechanisms.Results:PSC supernatant (PSC-SN) dose-dependently induced the trans-migration of Panc1 and UlaPaCa cells, mainly via haptokinesis and haptotaxis, respectively. In contrast to poly-L-lysine or fibronectin, collagen I resembled PSC-SN with respect to its effect on cancer cell behaviours, including polarised morphology, facilitated adhesion, accelerated motility and stimulated trans-migration. Blocking antibodies against integrin alpha2/beta1 subunits significantly attenuated PSC-SN- or collagen I-promoted cell trans-migration and adhesion. Moreover, both PSC-SN and collagen I induced the formation of F-actin and focal adhesions in cells, which was consistent with the constantly enhanced phosphorylation of focal adhesion kinase (FAK, Tyr397). Inhibition of FAK function by an inhibitor or small interference RNAs significantly diminished the effect of PSC-SN or collagen I on haptotaxis/haptokinesis of pancreatic cancer cells.Conclusion:Collagen I is the major mediator for PSC-SN-induced haptokinesis of Panc1 and haptotaxis of UlaPaCa by activating FAK signalling via binding to integrin alpha2beta1.British Journal of Cancer advance online publication, 7 November 2013; doi:10.1038/bjc.2013.706 www.bjcancer.com.

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[45]

TÍTULO / TITLE: - Surgery Indeed has an Important Role in Long-Term Outcome in Patients with Pancreatic Head Cancer.

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

REVISTA / JOURNAL: - World J Surg. 2013 Nov 26.

●● Enlace al texto completo (gratuito o de pago) 1007/s00268-013-2352-7

AUTORES / AUTHORS: - Zdravkovic D; Bilanovic D; Randjelovic T; Zdravkovic M; Dikic S

INSTITUCIÓN / INSTITUTION: - Surgery, Faculty of Medicine, University of Belgrade, Belgrade, Serbia, drdarkozdravkovic@gmail.com.

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[46]

TÍTULO / TITLE: - The Expression of PTEN Is Associated With Improved Prognosis in Patients With Ampullary Adenocarcinoma After Pancreaticoduodenectomy.

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

REVISTA / JOURNAL: - Arch Pathol Lab Med. 2013 Nov;137(11):1619-26. doi: 10.5858/arpa.2012-0418-OA.

●● Enlace al texto completo (gratuito o de pago) 5858/arpa.2012-0418-OA

AUTORES / AUTHORS: - Shroff S; Overman MJ; Rashid A; Shroff RT; Wang H; Chatterjee D; Katz MH; Lee JE; Wolff RA; Abbruzzese JL; Fleming JB; Wang H

INSTITUCIÓN / INSTITUTION: - From the Departments of Pathology (Drs S. Shroff, Rashid, and Huamin Wang), Gastrointestinal Medical Oncology (Drs Overman, R. T. Shroff, Hua Wang, Wolff, and Abbruzzese), and Surgical Oncology (Drs Chatterjee, Katz, Lee, and Fleming). The University of Texas M. D. Anderson Cancer Center, Houston.

RESUMEN / SUMMARY: - Context.-Phosphatase and tensin homolog (PTEN) is one of the most frequently inactivated tumor suppressor genes in sporadic cancers. Somatic mutations of PTEN occur in many tumors including those of the gastrointestinal and hepatobiliary tracts. Loss of PTEN expression is associated with poor prognosis in patients with metastatic colonic adenocarcinoma, gastroesophageal junction adenocarcinoma, gastric adenocarcinoma, and pancreatic ductal adenocarcinoma. Objective.-To study the expression of PTEN and its significance in ampullary adenocarcinoma (AA). Design.-We constructed tissue microarrays by using archival tissue from 92 patients (55 males, 37 females; median age, 63 years; age range, 37 to 87 years) with previously untreated AA who underwent pancreaticoduodenectomy at our institution. PTEN expression was evaluated by immunohistochemistry, scored semiquantitatively (based on staining intensity and percentage positive tumor cells), and correlated with clinicopathologic features and survival. Results.-Of 92 cases, 23 (25.0%) were PTEN negative. Loss of PTEN expression correlated with lymph node metastasis (P = .004), advanced American Joint Committee on Cancer (AJCC) stage (P = .02), and higher frequency of recurrence (P = .03). Patients with PTEN-negative tumors had shorter disease-free survival (DFS, mean: 89.0 +/- 20.8 months) and overall survival (OS, mean: 93.1 +/- 19.1 months) than those with PTEN-positive tumors (DFS, mean: 161.4 +/- 11.7 months, P = .01; OS, mean: 175.4 +/- 11.0 months, P = .001). In multivariate analyses, PTEN expression was a prognostic factor for both DFS and OS, independent of AJCC stage, lymph node status, pathologic tumor (pT) stage, and differentiation. Conclusions.-Loss of PTEN expression is associated with poor DFS and OS in patients with AA after curative surgery. PTEN expression may be used as a prognostic marker for patients with resected AA.

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[47]

TÍTULO / TITLE: - The case of a patient affected by primary gliosarcoma and neuroendocrine pancreatic cancer with prolonged survival.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Tumori. 2013 May-Jun;99(3):117e-9e. doi: 10.1700/1334.14818.
●● Enlace al texto completo (gratuito o de pago) 1700/1334.14818
AUTORES / AUTHORS: - Trignani M; Taraborrelli M; Ausili Cefaro G
RESUMEN / SUMMARY: - Primary gliosarcoma (PGS) is a rare neoplasm with a poor prognosis. It is considered as a variant of glioblastoma multiforme (GBM) and as a grade IV neoplasm. There is little evidence on the optimal therapy for this disease: treatment of PGS includes surgery, radiotherapy and chemotherapy, and often the same treatment used for GBM is employed for PGS. Several studies have demonstrated that somatostatin receptors are overexpressed in gliomas; somatostatin analogues could therefore also be employed in this mixed form but to date the experience reported in the literature is unclear and there are no studies about the use of these agents in PGS. We present the case of a patient affected by both PGS and neuroendocrine pancreatic cancer. The case is interesting for the prolonged survival and for the stabilization of disease obtained during therapy with somatostatin analogues.

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[48]
TÍTULO / TITLE: - Glycolytic ATP Fuels the Plasma Membrane Calcium Pump Critical for Pancreatic Cancer Cell Survival.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Biol Chem. 2013 Oct 24.
●● Enlace al texto completo (gratuito o de pago) 1074/jbc.M113.502948
AUTORES / AUTHORS: - James AD; Chan A; Erice Azparren O; Siriwardena AK; Bruce JI
INSTITUCIÓN / INSTITUTION: - The University of Manchester, United Kingdom;
RESUMEN / SUMMARY: - Pancreatic cancer is an aggressive cancer with poor prognosis and limited treatment options. Cancer cells rapidly proliferate and are resistant to cell death due, in part, to a shift from mitochondrial metabolism to glycolysis. We hypothesised that this shift is important in regulating cytosolic Ca2+ ([Ca2+]i), since the ATP-dependent plasma membrane Ca2+ ATPase (PMCA) is critical for maintaining low [Ca2+]i and thus cell survival. The present study aimed to determine the relative contribution of mitochondrial vs glycolytic ATP in fuelling the PMCA in human pancreatic cancer cells. We report that glycolytic inhibition induced profound ATP depletion, PMCA inhibition, [Ca2+]i overload and cell death in PANC1 and MIA PaCa-2 cells. Conversely, inhibition of mitochondrial metabolism had no effect, suggesting that glycolytic ATP is critical for [Ca2+]i homeostasis and thus survival. Targeting the glycolytic regulation of the PMCA may therefore be an effective strategy for selectively killing pancreatic cancer, whilst sparing healthy cells.

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[49]
TÍTULO / TITLE: - Safety and pharmacology of gemcitabine and capecitabine in patients with advanced pancreatico-biliary cancer and hepatic dysfunction.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Oct 29.
●● Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2327-2
AUTORES / AUTHORS: - Joerger M; Huitema AD; Koeberle D; Rosing H; Beijnen JH; Hitz F; Cerny T; Schellens JH; Gillessen S
INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology and Hematology, Cantonal Hospital, Rorschacherstrasse 95, 9007, St. Gallen, Switzerland, markus.joerger@gmail.com.
RESUMEN / SUMMARY: - PURPOSE: We assessed the impact of hepatic dysfunction on the safety and pharmacology of gemcitabine/capecitabine in patients with advanced pancreatico-biliary cancer. METHODS: We included 12 patients receiving 3 weekly gemcitabine 1,000 mg/m2 day 1, 8 and oral capecitabine 650 mg/m2 b.i.d. over 2 weeks until disease progression or intolerable toxicity. Patients were included into one normal hepatic function cohort [total bilirubin (TB) </=15 mumol/L] and 3 cohorts with increasing TB (16-39, 40-80, >80 mumol/L). Three patients with a creatinine clearance <60 ml/min were also included. Patients were sampled for gemcitabine, difluoro-deoxy uridine, intracellular gemcitabine triphosphates, capecitabine, 5'-deoxy-5-fluorocytidine, 5'-deoxy-5-fluorouridine and 5-fluorouracil up to 4 h after initiation of chemotherapy on day 1, and up to 90 min on day 8. All compounds were analyzed using validated liquid chromatography-tandem mass spectrometry. Nonlinear mixed-effect modeling was used for population analysis. RESULTS: Hepatic dysfunction was caused by intrahepatic cholestasis in 4 out of 8 patients (50 %) and extrahepatic cholestasis in another 4 patients (50 %). Dose-limiting toxicity was increasing hyperbilirubinemia and severe neutropenia in 2 patients each. Hepatic dysfunction was not associated with dose-limiting toxicity or severe hematological or non-hematological toxicity. However, hepatic dysfunction was associated with low clearance of both gemcitabine (p = 10-3) and capecitabine (p = 10-5), and low intracellular gemcitabine triphosphate concentrations (p = 10-3). CONCLUSIONS: Gemcitabine/capecitabine can be given at the standard dose in patients with severe hyperbilirubinemia, though the present data suggest that gemcitabine's activity may be limited due to poor intracellular activation. In patients with severe hyperbilirubinemia, initial monotherapy with capecitabine should be considered, followed by the addition of gemcitabine with improving hyperbilirubinemia.

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[50]
TÍTULO / TITLE: - Differences in disease expression between primary ciliary dyskinesia and cystic fibrosis with and without pancreatic insufficiency.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Chest. 2013 Oct 3. doi: 10.1378/chest.13-1162.
●● Enlace al texto completo (gratuito o de pago) 1378/chest.13-1162
AUTORES / AUTHORS: - Cohen-Cymberknoh M; Simanovsky N; Hiller N; Hillel AG; Shoseyov D; Kerem E
RESUMEN / SUMMARY: - ABSTRACT BACKGROUND: Impaired mucociliary clearance causes pulmonary disease in primary ciliary dyskinesia (PCD) and contributes to cystic fibrosis (CF) lung disease. Although the sino-pulmonary disease is similar, morbidity and mortality are different. Both PCD and CF-patients with pancreatic sufficiency (CF-PS) show no nutrient malabsorption and are diagnosed at a later age compared with

pancreatic-insufficient (CF-PI) patients. METHODS: Clinical status, microbiology, FEV1 and HRCT presented as total Brody score (CT-TBS) was compared for PCD, CF-PI and CF-PS patients, all treated at the same medical center, by the same team and by a similar routine follow-up. RESULTS: 164 patients, 34 PCD, 88 CF-PI, and 42 CF-PS were enrolled. PCD was diagnosed at a similar age as CF-PS, but significantly later than CF-PI. Mean FEV1% predicted was similar for the three groups. The rate of FEV1 change with age in PCD was similar to CF-PS, but significantly lower than in CF-PI. Severity of structural lung disease (CT-TBS) was similar for PCD and CF-PS, and significantly higher in CF-PI. No correlation between TBS or P. aeruginosa infection and FEV1 in PCD was seen whereas a negative correlation with FEV1 was observed for both CF groups. CONCLUSION: Although in our study PCD was similar to CF-PS, the lack of correlation between FEV1 and age, CT-TBS and P. aeruginosa infection in PCD suggests that impaired mucociliary clearance is not the only cause for inducing pulmonary damage in these diseases. Furthermore, a comparison of disease characteristics for PCD and CF should distinguish between CF-PI and CF-PS as different entities.

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[51]

TÍTULO / TITLE: - GLI1 interferes with the DNA mismatch repair system in pancreatic cancer through BHLHE41-mediated suppression of MLH1.

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

REVISTA / JOURNAL: - Cancer Res. 2013 Oct 28.

●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-13-2008

AUTORES / AUTHORS: - Inaguma S; Riku M; Hashimoto M; Murakami H; Saga S; Ikeda H; Kasai K

INSTITUCIÓN / INSTITUTION: - Pathology, Aichi Medical University School of Medicine.

RESUMEN / SUMMARY: - The mismatch repair (MMR) system is indispensable for the fidelity of DNA replication, the impairment of which predisposes to the development and progression of many types of cancers. To date, GLI1 transcription factor, a key molecule of the Hedgehog signaling pathway, has been showed to regulate the expression of several genes crucial for a variety of cancer cell properties in many types of cancers, including pancreatic ductal adenocarcinoma (PDAC), but whether GLI1 could control the MMR system was not known. Here we showed that GLI1 and GLI2 indirectly suppressed the expression of MLH1 in PDAC cells. Through GLI1-target gene screening, we found that GLI1 and GLI2 activated the expression of a basic-helix-loop-helix type suppressor BHLHE41 / DEC2 / SHARP1 through a GLI-binding site in the promoter. Consistent with a previous report that BHLHE41 suppresses the MLH1 promoter activity, we found that the activation of GLI1 led to the BHLHE41-dependent suppression of MLH1 and a double knockdown of GLI1 and GLI2 conversely increased the MLH1 protein in PDAC cells. Using TALEN-based modification of the MLH1 gene, we further showed that GLI1 expression was indeed associated with an increased tolerance to a methylating agent, N-methyl-N-nitrosourea (MNU), cooperatively with a lower copy number status of MLH1. Finally, GLI1 expression was immunohistochemically related positively with BHLHE41 and inversely with MLH1 in PDAC cells and precancerous lesions of the pancreas. Based on these

results, we propose that GLI1 depresses the MMR activity and might contribute to the development and progression of PDAC.

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[52]
TÍTULO / TITLE: - Regional Lymphadenectomy Is Indicated in the Surgical Treatment of Pancreatic Neuroendocrine Tumors (PNETs).
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Ann Surg. 2013 Nov 18.
●● Enlace al texto completo (gratuito o de pago)
1097/SLA.0000000000000348
AUTORES / AUTHORS: - Hashim YM; Trinkaus KM; Linehan DC; Strasberg SS; Fields RC; Cao D; Hawkins WG
INSTITUCIÓN / INSTITUTION: - *Department of Surgery and the Alvin J. Siteman Cancer Center, Barnes-Jewish Hospital and Washington University School of Medicine, St. Louis, MO daggerDivision of Biostatistics, Washington University School of Medicine, St. Louis, MO double daggerDepartment of Pathology and Immunology, Washington University School of Medicine, St Louis, MO, and Department of Pathology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital, Beijing, China.
RESUMEN / SUMMARY: - OBJECTIVE:: To explore the prognostic importance and preoperative predictors of lymph node metastasis in an effort to guide surgical decision making in patients with pancreatic neuroendocrine tumors (PNETs). BACKGROUND:: PNETs are uncommon, and the natural history of the disease is not well described. As a result, there remains controversy regarding the optimal management of regional lymph nodes during resection of the primary tumor. METHODS:: A retrospective review of a prospectively maintained database of patients who underwent surgery for locoregional PNET between 1994 and 2012 was performed. Logistic regression was used to identify predictors of nodal metastasis. Overall survival and disease-free survival were calculated using Kaplan-Meier method. Results were expressed as P values and odds ratio estimates, with 95% confidence intervals. RESULTS:: One hundred thirty-six patients were identified, of whom 50 (38%) patients had nodal metastasis. The frequency of lymph node metastasis was higher for larger tumors [> 1.5 cm (odds ratio [OR] = 4.7)], tumors of the head as compared with body-tail of the pancreas (OR = 2.8), tumors with Ki-67 greater than 20% (OR = 6.7), and tumors with lymph vascular invasion (OR = 3.6) ($P < 0.05$). Median disease-free survival was lower for patients with nodal metastases (4.5 vs 14.6 years, $P < 0.0001$). CONCLUSIONS:: Lymph node metastasis is predictive of poor outcomes in patients with PNETs. Preoperative variables are not able to reliably predict patients where the probability of lymph node involvement was less than 12%. These data support inclusion of regional lymphadenectomy in patients undergoing pancreatic resections for PNET.

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[53]
TÍTULO / TITLE: - Combination Treatment of Human Pancreatic Cancer Xenograft Models with the Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor Erlotinib and Oncolytic Herpes Simplex Virus HF10.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Oct 30.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3329-3

AUTORES / AUTHORS: - Yamamura K; Kasuya H; Sahin TT; Tan G; Hotta Y; Tsurumaru N; Fukuda S; Kanda M; Kobayashi D; Tanaka C; Yamada S; Nakayama G; Fujii T; Sugimoto H; Koike M; Nomoto S; Fujiwara M; Tanaka M; Kodera Y

INSTITUCIÓN / INSTITUTION: - Department of Surgery II, Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan.

RESUMEN / SUMMARY: - BACKGROUND: There is the potential to use replication-competent oncolytic viruses to treat cancer. We evaluated the efficacy of HF10, a herpes simplex virus type 1 (HSV-1) mutant, in combination with erlotinib, an epidermal growth factor receptor tyrosine kinase inhibitor, in human pancreatic cancer xenograft models. METHODS: The viability of human pancreatic cancer cell lines (BxPC-3 and PANC-1) treated with HF10 and erlotinib, on their own or in combination, was determined. Effects of erlotinib on HF10 entry into tumor cells were also investigated. BxPC-3 subcutaneous tumor-bearing mice were treated with HF10 and erlotinib, on their own or in combination, with effects on tumor volume determined. Immunohistochemical examination of HSV-1 and CD31 was conducted to assess virus distribution and angiogenesis within tumors. A peritoneally disseminated BxPC-3 xenograft model was evaluated for survival. RESULTS: HF10 combined with erlotinib demonstrated the highest cytotoxicity against BxPC-3. A combination effect was not observed in PANC-1 cells, and erlotinib did not affect virus entry into tumor cells. In the peritoneally disseminated model, HF10 combined with erlotinib had no beneficial effect on survival. In the subcutaneous tumor model, combination therapy resulted in the inhibition of tumor growth to a greater extent than using each agent on its own. Immunohistochemistry revealed that virus distribution within the tumor persisted in the combination therapy group. CONCLUSIONS: Combination therapy with HF10 and erlotinib warrants further investigation to establish a new treatment strategy against human pancreatic cancers.

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[54]

TÍTULO / TITLE: - Intraoperative irrigation cytology of the remnant pancreas to detect remnant distinct pancreatic ductal adenocarcinoma in patients with intraductal papillary mucinous neoplasm undergoing partial pancreatectomy.

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

REVISTA / JOURNAL: - Surgery. 2013 Oct 29. pii: S0039-6060(13)00381-4. doi: 10.1016/j.surg.2013.06.059.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.06.059

AUTORES / AUTHORS: - Mori Y; Ohtsuka T; Tamura K; Ideno N; Aso T; Kono H; Nagayoshi Y; Ueda J; Takahata S; Aishima S; Ookubo F; Oda Y; Tanaka M

INSTITUCIÓN / INSTITUTION: - Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Patients with intraductal papillary mucinous neoplasm (IPMN) of the pancreas may have concomitant distinct pancreatic ductal adenocarcinoma (PDAC). We evaluated the safety and usefulness of intraoperative irrigation cytology of the remnant pancreas (IICP) during pancreatectomy to detect remnant distinct PDAC in patients with IPMN. METHODS: The records of all 48 patients with IPMN who underwent IICP during partial pancreatectomy at our institution

from April 2007 to March 2012 were reviewed retrospectively. After division of the pancreas, a 4-French tube was inserted into the main pancreatic duct of the remnant pancreas from the cut edge, and fluid for cytologic examination was obtained by saline irrigation through the tube. If the third IICP was positive, patients underwent additional pancreatic resection. Clinical and pathologic outcomes were evaluated. RESULTS: The third IICP was positive in 5 patients. Postoperative pathologic examination showed that these patients all had remnant distinct PDAC in the additionally resected specimen, which was not detectable on preoperative imaging examination or on intraoperative macroscopic examination, ultrasonography, or palpation. This PDAC was stage 0 in 4 patients and stage III in 1 patient. No procedure-related complications were observed. One patient developed peritoneal metastasis after 10 months, 1 developed liver metastasis after 20 months, and 1 developed PDAC in the remnant pancreas after 24 months. CONCLUSION: IICP seems to be a safe and useful method for detection of early stage PDAC concomitant with IPMN that cannot be detected by preoperative imaging or intraoperative examination.

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[55]

TÍTULO / TITLE: - Interleukin-6 is required for pancreatic cancer progression by promoting MAPK signaling activation and oxidative stress resistance.

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

REVISTA / JOURNAL: - Cancer Res. 2013 Oct 15;73(20):6359-74. doi: 10.1158/0008-5472.CAN-13-1558-T. Epub 2013 Oct 4.

●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-13-1558-T

AUTORES / AUTHORS: - Zhang Y; Yan W; Collins MA; Bednar F; Rakshit S; Zetter BR; Stanger BZ; Chung I; Rhim AD; di Magliano MP

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of Surgery, Pathology, and Cell and Developmental Biology, Department of Internal Medicine-Gastroenterology, Michigan Center for Translational Pathology, Program in Cellular and Molecular Biology, Comprehensive Cancer Center, University of Michigan, Ann Arbor, Michigan; Vascular Biology Program, Department of Surgery, Karp Family Research Laboratories, Children's Hospital, Boston, Massachusetts; Gastroenterology Division, Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; Department of Pharmacology, and University of Malaya Cancer Research Institute, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia.

RESUMEN / SUMMARY: - Pancreatic cancer, one of the deadliest human malignancies, is almost invariably associated with the presence of an oncogenic form of Kras. Mice expressing oncogenic Kras in the pancreas recapitulate the stepwise progression of the human disease. The inflammatory cytokine interleukin (IL)-6 is often expressed by multiple cell types within the tumor microenvironment. Here, we show that IL-6 is required for the maintenance and progression of pancreatic cancer precursor lesions. In fact, the lack of IL-6 completely ablates cancer progression even in presence of oncogenic Kras. Mechanistically, we show that IL-6 synergizes with oncogenic Kras to activate the reactive oxygen species detoxification program downstream of the mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK) signaling cascade. In addition, IL-6 regulates the inflammatory microenvironment of

pancreatic cancer throughout its progression, providing several signals that are essential for carcinogenesis. Thus, IL-6 emerges as a key player at all stages of pancreatic carcinogenesis and a potential therapeutic target.

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[56]

TÍTULO / TITLE: - Crizotinib Inhibits Metabolic Inactivation of Gemcitabine in c-Met-driven Pancreatic Carcinoma.

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

REVISTA / JOURNAL: - Cancer Res. 2013 Nov 15;73(22):6745-56. doi: 10.1158/0008-5472.CAN-13-0837. Epub 2013 Oct 1.

●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-13-0837

AUTORES / AUTHORS: - Avan A; Caretti V; Funel N; Galvani E; Maftouh M; Honeywell RJ; Lagerweij T; Van Tellingen O; Campani D; Fuchs D; Verheul HM; Schuurhuis GJ; Boggi U; Peters GJ; Wurdinger T; Giovannetti E

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of Medical Oncology, Hematology, Neurosurgery and Pediatric Oncology/Hematology, Neuro-oncology Research Group, VU University Medical Center; Diagnostic Oncology Division, Netherlands Cancer Institute; VisualSonics, Amsterdam, the Netherlands; Departments of Neurology and Pediatrics, Stanford University School of Medicine, Stanford, California; Division of Surgical Pathology, Division of General and Transplant Surgery, University of Pisa, Pisa, Italy; and Molecular Neurogenetics Unit, Department of Neurology, Massachusetts General Hospital and Neuroscience Program, Harvard Medical School, Boston, Massachusetts.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) remains a major unsolved health problem. Most drugs that pass preclinical tests fail in these patients, emphasizing the need of improved preclinical models to test novel anticancer strategies. Here, we developed four orthotopic mouse models using primary human PDAC cells genetically engineered to express firefly- and Gaussia luciferase, simplifying the ability to monitor tumor growth and metastasis longitudinally in individual animals with MRI and high-frequency ultrasound. In these models, we conducted detailed histopathologic and immunohistochemical analyses on paraffin-embedded pancreatic tissues and metastatic lesions in liver, lungs, and lymph nodes. Genetic characteristics were compared with the originator tumor and primary tumor cells using array-based comparative genomic hybridization, using frozen specimens obtained by laser microdissection. Notably, the orthotopic human xenografts in these models recapitulated the phenotype of human PDACs, including hypovascular and hypoxic areas. Pursuing genomic and immunohistochemical evidence revealed an increased copy number and overexpression of c-Met in one of the models; we examined the preclinical efficacy of c-Met inhibitors in vitro and in vivo. In particular, we found that crizotinib decreased tumor dimension, prolonged survival, and increased blood and tissue concentrations of gemcitabine, synergizing with a cytidine deaminase-mediated mechanism of action. Together, these more readily imaged orthotopic PDAC models displayed genetic, histopathologic, and metastatic features similar to their human tumors of origin. Moreover, their use pointed to c-Met as a candidate therapeutic target in PDAC and highlighted crizotinib and gemcitabine as a synergistic combination of

drugs warranting clinical evaluation for PDAC treatment. Cancer Res; 73(22); 6745-56. ©2013 AACR.

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[57]

TÍTULO / TITLE: - Circulating IL-35 in pancreatic ductal adenocarcinoma patients.

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

REVISTA / JOURNAL: - Hum Immunol. 2013 Oct 11. pii: S0198-8859(13)00562-4. doi: 10.1016/j.humimm.2013.09.018.

●● Enlace al texto completo (gratuito o de pago) 1016/j.humimm.2013.09.018

AUTORES / AUTHORS: - Jin P; Ren H; Sun W; Xin W; Zhang H; Hao J

INSTITUCIÓN / INSTITUTION: - Department of Pancreatic Cancer, Key Lab of Cancer Treatment and Prevention, Tianjin Cancer Hospital, Tianjin Medical University, Tianjin 300060, China.

RESUMEN / SUMMARY: - IL-35 is a novel inhibitory cytokine that is mainly produced by regulatory T-cells (Tregs) and is required for Treg-mediated immunosuppression. However, the plasma levels of IL-35 in patients with pancreatic ductal adenocarcinoma (PDAC) have never been investigated. In this study, we found that plasma IL-35 levels more significantly increased in PDAC patients than in normal controls (134.53+/-92.45pg/mL vs. 14.26+/-6.56pg/mL). IL-35 mRNA levels were positively correlated with plasma IL-35 levels (EBI3, R=0.925, p<0.01; p35, R=0.916, p<0.01). Furthermore, IL-35 expression levels were associated with lymph node metastasis (p=0.001) and late tumor stage (p=0.002). For the resected patients, high IL-35 expression levels were associated with large tumor size (p<0.01), higher TNM classification T staging (p<0.05), and late tumor stage (p<0.05). In conclusion, circulating IL-35 in PDAC patients significantly increased, suggesting that regulating the expression of IL-35 may provide a new possible target for the treatment of PDAC patients, especially for the resectable ones.

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[58]

TÍTULO / TITLE: - Targeting microRNAs in Pancreatic Cancer: Microplayers in the Big Game.

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

REVISTA / JOURNAL: - Cancer Res. 2013 Nov 15;73(22):6541-7. doi: 10.1158/0008-5472.CAN-13-1288. Epub 2013 Nov 7.

●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-13-1288

AUTORES / AUTHORS: - Khan S; Ansarullah; Kumar D; Jaggi M; Chauhan SC

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Department of Pharmaceutical Sciences and Center for Cancer Research, University of Tennessee Health Science Center, Memphis, Tennessee; The Sanford Project, Children Health Research Center, Sanford Research/USD, Sioux Falls, South Dakota; and Cancer Research Laboratory, Department of Biological and Environmental Sciences, University of the District of Columbia, Washington, District of Columbia.

RESUMEN / SUMMARY: - The prognosis of patients with pancreatic cancer is extremely poor, and current systemic therapies result in only marginal survival rates for patients. The era of targeted therapies has offered a new avenue to search for more effective

therapeutic strategies. Recently, microRNAs (miRNA) that are small noncoding RNAs (18-24 nucleotides) have been associated with a number of diseases, including cancer. Disruption of miRNAs may have important implications in cancer etiology, diagnosis, and treatment. So far, focus has been on the mechanisms that are involved in translational silencing of their targets to fine tune gene expression. This review summarizes the approach for rational validation of selected candidates that might be involved in pancreatic tumorigenesis, cancer progression, and disease management. Herein, we also focus on the major issues hindering the identification of miRNAs, their linked pathways and recent advances in understanding their role as diagnostic/prognostic biomarkers, and therapeutic tools in dealing with this disease. miRNAs are expected to be robust clinical analytes, valuable for clinical research and biomarker discovery. Cancer Res; 73(22); 6541-7. ©2013 AACR.

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[59]

TÍTULO / TITLE: - Diabetes type II, other medical conditions and pancreatic cancer risk: a prospective study in The Netherlands.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 26;109(11):2924-32. doi: 10.1038/bjc.2013.629. Epub 2013 Oct 22.

●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.629

AUTORES / AUTHORS: - Eijgenraam P; Heinen MM; Verhage BA; Keulemans YC; Schouten LJ; van den Brandt PA

INSTITUCIÓN / INSTITUTION: - 1] School for Oncology and Developmental Biology (GROW), Department of Epidemiology, Maastricht University Medical Centre+, Peter Debyeplein 1, 6229 HA, Maastricht, The Netherlands [2] Department of Biochemistry, Maastricht University Medical Centre+, Universiteitssingel 50, 6229 ER, Maastricht, The Netherlands.

RESUMEN / SUMMARY: - Background:To date, only a few risk factors for pancreatic cancer have been established. We examined prospectively relations between several medical conditions and pancreatic cancer incidence.Methods:In 1986, 120 852 participants completed a baseline questionnaire on cancer risk factors, including several self-reported physician diagnosed medical conditions. At baseline, a random subcohort of 5000 participants was selected using a case-cohort approach for analysis. After 16.3 years of follow-up, 448 pancreatic cancer cases (63% microscopically confirmed) were available for analysis.Results:Diabetes mellitus type II and hepatitis were positively associated with pancreatic cancer risk (multivariable-adjusted hazard ratio: 1.79; 95% confidence interval: 1.12-2.87 and hazard ratio: 1.37; 95% confidence interval: 1.04-1.81, respectively). Furthermore, a positive trend in risk with increasing years of diagnosis of diabetes (P=0.004) and of hepatitis (P=0.02) was observed. However, an inverse association was observed between hypertension and pancreatic cancer risk, this was found among microscopically confirmed cases only (hazard ratio: 0.66; 95% confidence interval: 0.49-0.90), while years since diagnosis of hypertension significantly decreased cancer risk (P for trend=0.02).Conclusion:In this prospective study, a positive association was observed between self-reported physician diagnosed diabetes mellitus type II and hepatitis and pancreatic cancer risk, whereas an inverse association was observed with hypertension.

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[60]

TÍTULO / TITLE: - Heat-shock protein 90 inhibitors synergistically enhance melanoma differentiation-associated gene-7-mediated cell killing of human pancreatic carcinoma.

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

REVISTA / JOURNAL: - Cancer Gene Ther. 2013 Nov 22. doi: 10.1038/cgt.2013.66.

●● Enlace al texto completo (gratuito o de pago) 1038/cgt.2013.66

AUTORES / AUTHORS: - Zhang Z; Kawamura K; Jiang Y; Shingyoji M; Ma G; Li Q; Hu J; Qi Y; Liu H; Zhang F; Kang S; Shan B; Wang S; Chada S; Tagawa M

INSTITUCIÓN / INSTITUTION: - 1] Division of Pathology and Cell Therapy, Chiba Cancer Center Research Institute, Chuo-ku, Chiba, Japan [2] Department of Gynecology and Obstetrics, The Fourth Hospital of Hebei Medical University, Shijiazhuang, China.

RESUMEN / SUMMARY: - Pancreatic cancer is one of the intractable diseases and an effective therapeutic strategy is required to improve the prognosis. We examined possible antitumor effects of adenoviruses expressing melanoma differentiation-associated gene-7/interleukin-24 (Ad-mda-7) and a heat-shock protein 90 (Hsp90) inhibitor to human pancreatic carcinoma cells. Ad-mda-7 and an Hsp90 inhibitor, geldanamycin (GA), produced cytotoxic effects, and a combinatory use of Ad-mda-7 and GA further achieved synergistic effects. Administration of N-acetyl-L-cysteine, an inhibitor of reactive oxygen species, eliminated Ad-mda-7- and GA-mediated cytotoxicity. Ad-mda-7 augmented phosphorylated AKT levels but GA did not influence the phosphorylation. GA-treated cells showed cleavage of poly-(ADP-ribose) polymerase but not caspase-3, and upregulated Hsp70 and LC3A/B II levels, whereas Ad-mda-7-treated cells did not. GA treatments augmented ubiquitination and markedly increased melanoma differentiation-associated gene-7 (MDA-7) expression levels. These findings suggest that Ad-mda-7-mediated cytotoxicity is dependent on reactive oxygen species but independent of apoptosis or autophagy, and that GA-mediated cytotoxicity was linked with caspase-independent apoptosis and/or autophagy. A mechanism underlying the combinatory effects of Ad-mda-7 and GA remained complex and the synergism is attributable to multiple factors including increased MDA-7 protein stability by GA.Cancer Gene Therapy advance online publication, 22 November 2013; doi:10.1038/cgt.2013.66.

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[61]

TÍTULO / TITLE: - Epithelial splicing regulatory protein 1 is a favorable prognostic factor in pancreatic cancer that attenuates pancreatic metastases.

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

REVISTA / JOURNAL: - Oncogene. 2013 Sep 30. doi: 10.1038/onc.2013.392.

●● Enlace al texto completo (gratuito o de pago) 1038/onc.2013.392

AUTORES / AUTHORS: - Ueda J; Matsuda Y; Yamahatsu K; Uchida E; Naito Z; Korc M; Ishiwata T

INSTITUCIÓN / INSTITUTION: - 1] Departments of Pathology and Integrative Oncological Pathology, Nippon Medical School, Tokyo, Japan [2] Department of Surgery for Organ and Biological Regulation, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan.

RESUMEN / SUMMARY: - Epithelial splicing regulatory protein 1 (ESRP1) binds the FGFR-2 auxiliary cis-element ISE/ISS-3, located in the intron between exon IIIb and IIIc, and primarily promotes FGFR-2 IIIb expression. Here we assessed the role of ESRP1 in pancreatic ductal adenocarcinoma (PDAC). Immunohistochemical analysis was performed using anti-ESRP1, FGFR-2 IIIb and FGFR-2 IIIc antibodies in 123 PDAC cases. ESRP1 expression vector and small interference RNA (siRNA) targeting ESRP1 were transfected into human PDAC cells, and cell growth, migration and invasion were analyzed. In vivo heterotopic and orthotopic implantations using ESRP1 overexpression clones were performed and effects on pancreatic tumor volumes and hepatic and pulmonary metastases determined. ESRP1 immunoreactivity was strong in the nuclei of cancer cells in well-to-moderately differentiated PDACs but weak in poorly differentiated cancers. Well-to-moderately differentiated cancers also exhibited high FGFR-2 IIIb and low FGFR-2 IIIc expression, whereas this ratio was reversed in the poorly differentiated cancers. Increased ESRP1 expression was associated with longer survival in comparison with low ESRP1 expression, and PANC-1 cells engineered to express ESRP1 exhibited increased FGFR-2 IIIb expression and decreased migration and invasion in vitro, whereas ESRP1 siRNA-transfected KLM-1 cells exhibited increased FGFR-2 IIIc expression and increased cell growth, migration and invasion. In vivo, ESRP1-overexpressing clones formed significantly fewer liver metastases as compared with control clones. ESRP1 regulates the expression pattern of FGFR-2 isoforms, attenuates cell growth, migration, invasion and metastasis, and is a favorable prognostic factor in PDAC. Therefore, devising mechanisms to upregulate ESRP1 may exert a beneficial therapeutic effect in PDAC.Oncogene advance online publication, 30 September 2013; doi:10.1038/onc.2013.392.

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[62]

TÍTULO / TITLE: - Etoposide induces apoptosis via the mitochondrial- and caspase-dependent pathways and in non-cancer stem cells in Panc-1 pancreatic cancer cells.

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

REVISTA / JOURNAL: - Oncol Rep. 2013 Dec;30(6):2765-70. doi: 10.3892/or.2013.2767. Epub 2013 Oct 1.

●● Enlace al texto completo (gratuito o de pago) 3892/or.2013.2767

AUTORES / AUTHORS: - Zhang SH; Huang Q

INSTITUCIÓN / INSTITUTION: - Experimental Research Center, First People's Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai 200080, P.R. China.

RESUMEN / SUMMARY: - Pancreatic cancer is a highly aggressive malignant tumor. In the present study, we performed several methods, including CCK-8 assay, immunofluorescence technique, western blotting and flow cytometry, to determine the effects of VP16 (etoposide) on Panc-1 pancreatic cancer cells. The results demonstrated that VP16 inhibited the growth of and induced apoptosis in Panc-1 cells. Western blot analysis showed that VP16 inhibited the expression of Bcl-2 and enhanced the expression of Bax, caspases-3 and -9, cytochrome c and PARP. Notably, a strong inhibitory effect of VP16 on Panc-1 cells mainly occurred in non-CSCs. These data provide a new strategy for the therapy of pancreatic cancer.

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[63]

TÍTULO / TITLE: - Efficacy of percutaneous transhepatic cholangiodrainage (PTCD) in patients with unresectable pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 22.
●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-1363-1
AUTORES / AUTHORS: - Wu J; Song L; Zhang Y; Zhao DY; Guo B; Liu J
INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, The Second Hospital of Dalian Medical University, Dalian, 116027, China.
RESUMEN / SUMMARY: - For patients with pancreatic cancer who suffer from obstructive jaundice, percutaneous transhepatic cholangiodrainage (PTCD) is the treatment of choice. However, there are no standards for palliative care for patients undergoing this treatment. The aim of this study was to retrospectively evaluate the efficacy of post-palliative treatment in patients with unresectable pancreatic cancer who were previously treated with PTCD. The 47 patients included in this study had unresectable pancreatic cancer, presented with obstructive jaundice, had no prior history of chemotherapy, and underwent PTCD. They were divided into two groups. Group A was composed of 21 patients who received post-palliative treatment (chemotherapy, radiation, or chemoradiotherapy). Group B consisted of 26 patients who were under best supportive care (BSC). We compared the median overall survival time between the two groups to evaluate the efficacy of post-palliative treatment. The median overall survival time (MOST) of patients undergoing PTCD was 7.19 months. MOST was 9.07 months for patients in group A (P = 0.017 vs. group B) and 5.52 months for those in group B. Among the patients receiving post-palliative treatment, 12 (57 % of patients) received only a single therapy (either chemo or radiation), and 9 (43 %) received chemoradiotherapy. Their median overall survival times were 8.31 and 11.15 months, respectively (P = 0.325). Post-palliative treatment in patients with unresectable pancreatic cancer previously treated with PTCD is more effective than only best supportive care alone. Patients receiving both chemo and radiation may benefit more in terms of overall survival compared to patients receiving only one or the other.

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[64]
TÍTULO / TITLE: - Triptolide-induced Cell Death in Pancreatic Cancer Is Mediated by O-GlcNAc Modification of Transcription Factor Sp1.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Biol Chem. 2013 Nov 22;288(47):33927-38. doi: 10.1074/jbc.M113.500983. Epub 2013 Oct 15.
●● Enlace al texto completo (gratuito o de pago) 1074/jbc.M113.500983
AUTORES / AUTHORS: - Banerjee S; Sangwan V; McGinn O; Chugh R; Dudeja V; Vickers SM; Saluja AK
INSTITUCIÓN / INSTITUTION: - From the Division of Basic and Translational Research, Department of Surgery, and.
RESUMEN / SUMMARY: - Pancreatic cancer, the fourth most prevalent cancer-related cause of death in the United States, is a disease with a dismal survival rate of 5% 5 years after diagnosis. One of the survival proteins responsible for its extraordinary ability to evade cell death is HSP70. A naturally derived compound, triptolide, and its water-soluble prodrug, Minnelide, down-regulate the expression of this protein in

pancreatic cancer cells, thereby causing cell death. However, the mechanism of action of triptolide has not been elucidated. Our study shows that triptolide-induced down-regulation of HSP70 expression is associated with a decrease in glycosylation of the transcription factor Sp1. We further show that triptolide inhibits glycosylation of Sp1, inhibiting the hexosamine biosynthesis pathway, particularly the enzyme O-GlcNAc transferase. Inhibition of O-GlcNAc transferase prevents nuclear localization of Sp1 and affects its DNA binding activity. This in turn down-regulates prosurvival pathways like NF-kappaB, leading to inhibition of HSF1 and HSP70 and eventually to cell death. In this study, we evaluated the mechanism by which triptolide affects glycosylation of Sp1, which in turn affects downstream pathways controlling survival of pancreatic cancer cells.

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[65]

TÍTULO / TITLE: - Human Pancreatic Cancer Cells with Acquired Gemcitabine Resistance Exhibit Significant Up-regulation of Peroxiredoxin-2 Compared to Sensitive Parental Cells.

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

REVISTA / JOURNAL: - Anticancer Res. 2013 Nov;33(11):4821-6.

AUTORES / AUTHORS: - Suenaga S; Kuramitsu Y; Wang Y; Baron B; Kitagawa T; Akada J; Tokuda K; Kaino S; Maehara S; Maehara Y; Sakaida I; Nakamura K

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Functional Proteomics, Yamaguchi University Graduate School of Medicine, 1-1-1 Minami-Kogushi, Ube, Yamaguchi 755-8505, Japan. climates@yamaguchi-u.ac.jp.

RESUMEN / SUMMARY: - Gemcitabine (2'-deoxy-2'-difluorodeoxycytidine) is the only clinically effective drug for pancreatic cancer. However, high levels of inherent and acquired tumor resistance to gemcitabine lead to difficulty of chemotherapy for pancreatic cancer. We have reported on a proteomic study of gemcitabine-sensitive KLM1 and -resistant KLM1-R pancreatic cancer cells, and identified some proteins which were shown to be up-regulated in KLM1-R compared to KLM1 cells. In those proteomic studies, peroxiredoxin-2 was listed as an up-regulated protein in KLM1-R cells. Peroxiredoxin-2 is a member of a family of peroxiredoxins providing a protective role for redox damage. In this study, the expression of peroxiredoxin-2 in KLM1 and KLM1-R cells was compared. It was found that peroxiredoxin-2 was significantly up-regulated in KLM1-R cells compared to KLM1 cells ($p<0.001$). However, peroxiredoxin-1 expression was significantly down-regulated in KLM1-R cells ($p<0.001$). These results suggest that peroxiredoxin-2 is a possible candidate biomarker for predicting the response of patients with pancreatic cancer to treatment with gemcitabine.

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[66]

TÍTULO / TITLE: - KPNA7, a nuclear transport receptor, promotes malignant properties of pancreatic cancer cells in vitro.

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

REVISTA / JOURNAL: - Exp Cell Res. 2013 Nov 23. pii: S0014-4827(13)00502-8. doi: 10.1016/j.yexcr.2013.11.014.

●● Enlace al texto completo (gratuito o de pago) 1016/j.yexcr.2013.11.014

AUTORES / AUTHORS: - Laurila E; Vuorinen E; Savinainen K; Rauhala H; Kallioniemi A

INSTITUCIÓN / INSTITUTION: - Institute of Biomedical Technology, FIN-33014 University of Tampere and BioMediTech, Biokatu 6, 33520 Tampere, Finland; Fimlab Laboratories, Biokatu 4, 33520 Tampere, Finland.

RESUMEN / SUMMARY: - Pancreatic cancer is an aggressive malignancy and one of the leading causes of cancer deaths. The high mortality rate is mostly due to the lack of appropriate tools for early detection of the disease and a shortage of effective therapies. We have previously shown that karyopherin alpha 7 (KPNA7), the newest member of the alpha karyopherin family of nuclear import receptors, is frequently amplified and overexpressed in pancreatic cancer. Here, we report that KPNA7 expression is absent in practically all normal human adult tissues but elevated in several pancreatic cancer cell lines. Inhibition of KPNA7 expression in AsPC-1 and Hs700T pancreatic cancer cells led to a reduction in cell growth and decreased anchorage independent growth, as well as increased autophagy. The cell growth effects were accompanied by an induction of the cell cycle regulator p21 and a G1 arrest of the cell cycle. Interestingly, the p21 induction was caused by increased mRNA synthesis and not defective nuclear transport. These data strongly demonstrate that KPNA7 silencing inhibits the malignant properties of pancreatic cancer cells in vitro and thereby provide the first evidence on the functional role for KPNA7 in human cancer.

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[67]

TÍTULO / TITLE: - Genetic Variability in Energy Balance and Pancreatic Cancer Risk in a Population-Based Case-Control Study in Minnesota.

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

REVISTA / JOURNAL: - Pancreas. 2013 Nov 6.

●● Enlace al texto completo (gratuito o de pago)

1097/MPA.0b013e3182a7c829

AUTORES / AUTHORS: - Zhang J; Dhakal IB; Zhang X; Prizment AE; Anderson KE

INSTITUCIÓN / INSTITUTION: - From the *Department of Epidemiology, Indiana University Richard M. Fairbanks School of Public Health at IUPUI; daggerMelvin Bren Simon Cancer Center, Indiana University, Indianapolis, IN; double daggerDepartment of Biostatistics, Fay W. Boozman College of Public Health, University of Arkansas for Medical Sciences, Little Rock, AR; section signDepartment of Molecular Biology, College of Life Sciences, Hebei United University, Tangshan, China; parallelDivision of Epidemiology and Community Health, School of Public Health, and paragraph signMasonic Cancer Center, University of Minnesota, Minneapolis, MN.

RESUMEN / SUMMARY: - OBJECTIVES: Accumulating evidence suggests that energy imbalance plays a role in pancreatic carcinogenesis. However, it remains unclear whether single-nucleotide polymorphisms (SNPs) in genes regulating energy homeostasis influence pancreatic cancer risk. We investigated this question in a case-control study conducted from 1994 to 1998. METHODS: Patients (n = 173) were ascertained from hospitals in the Twin Cities and Mayo Clinic, Minnesota. Control subjects (n = 476) were identified from the general population and frequency matched to patients by age and sex. Seven SNPs were evaluated in relation to pancreatic cancer using unconditional logistic regression. RESULTS: After adjustment for confounders, the leucine/proline or proline/proline genotype of the neuropeptide Y

(NPY) gene rs16139 was associated with a lower risk than the leucine/leucine genotype (odds ratio, 0.40 [95% confidence interval, 0.15-0.91]). Conversely, an increased risk was observed for the glycine/arginine or arginine/arginine genotype of the adrenoceptor beta2, surface (ADRB2) gene rs1042713 as compared with the glycine/glycine genotype (odds ratio, 1.52 [95% confidence interval, 1.01-2.31]). CONCLUSIONS: This study first reveals that SNPs in genes modulating energy intake (NPY) and energy expenditure (ADRB2) altered pancreatic cancer risk. If confirmed by other studies, our findings may shed new light on the etiology and prevention of pancreatic cancer.

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[68]
TÍTULO / TITLE: - The combination of the serum carbohydrate antigen 19-9 and carcinoembryonic antigen is a simple and accurate predictor of mortality in pancreatic cancer patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Surg Today. 2013 Oct 9.
●● Enlace al texto completo (gratuito o de pago) 1007/s00595-013-0752-9
AUTORES / AUTHORS: - Kanda M; Fujii T; Takami H; Suenaga M; Inokawa Y; Yamada S; Nakayama G; Sugimoto H; Koike M; Nomoto S; Kodera Y
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery (Surgery II), Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, 466-8550, Japan.
RESUMEN / SUMMARY: - PURPOSE: The aim of this study was to detect high-performance prognostic biomarkers of pancreatic cancer which would enable the identification of high-risk patients. METHODS: The subjects were 324 patients who underwent radical surgery for pancreatic ductal adenocarcinoma without neoadjuvant therapy. We evaluated the prognostic impact of four perioperative serum tumor markers, including carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA). We also evaluated the indices by multiplying the values of two tumor markers (e.g., CA19-9 x CEA). RESULTS: The preoperative CA19-9 x CEA index had a strong correlation with the prognosis of patients with pancreatic cancer, even when the cut-off was set at the median value. CA19-9 x CEA >/=500 was an independent predictor of mortality (hazard ratio: 1.642, p = 0.021). In the ROC curve analysis of early mortality after surgery, the CA19-9 x CEA index had the highest goodness of fit. The presence of CA19-9 x CEA >/=500 had the largest attributable risk proportion because of its combined high predictive performance and prevalence. The postoperative CA19-9 x CEA index was also a significant predictive marker of mortality. CONCLUSION: The CA19-9 x CEA index is a strong prognostic biomarker that could help identify pancreatic cancer patients expected to have a poor prognosis so that they can be administered appropriate multidisciplinary treatment.

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[69]
TÍTULO / TITLE: - Value of EUS in early detection of pancreatic ductal adenocarcinomas in patients with intraductal papillary mucinous neoplasms.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Endoscopy. 2013 Nov 11.

●● Enlace al texto completo (gratuito o de pago) 1055/s-0033-1353603

AUTORES / AUTHORS: - Kamata K; Kitano M; Kudo M; Sakamoto H; Kadosaka K; Miyata T; Imai H; Maekawa K; Chikugo T; Kumano M; Hyodo T; Murakami T; Chiba Y; Takeyama Y

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology and Hepatology, Kinki University Faculty of Medicine, Osaka-sayama, Japan.

RESUMEN / SUMMARY: - Background and study aims: Pancreatic ductal adenocarcinomas (PDAC) sometimes arise in patients with intraductal papillary mucinous neoplasms (IPMNs). This study examined the incidence of PDACs concomitant to or derived from branch duct IPMNs. The usefulness of endoscopic ultrasonography (EUS) relative to other imaging methods for detecting these tumors was also assessed. Patients and methods: This retrospective study used data from clinical records and imaging studies that were collected prospectively. During 2001 - 2009, 167 consecutive patients with IPMNs underwent EUS, ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI). The 102 patients whose branch duct IPMNs lacked mural nodules/symptoms and thus did not qualify for resection were followed up by semiannual EUS and annual ultrasonography, CT, and MRI. The sensitivity and specificity with which the four modalities detected IPMN-derived and -concomitant PDACs at the first examination and throughout the study period were evaluated. The rate of PDAC development during follow-up was analyzed by the Kaplan-Meier method. Results: A total of 17 IPMN-derived and 11 IPMN-concomitant PDACs were diagnosed at the first examination. Lesions that did not qualify for resection or chemotherapy were followed up for a median of 42 months. Seven IPMN-concomitant PDACs and no IPMN-derived PDACs were detected during follow-up. The 3- and 5-year rates of IPMN-concomitant PDAC development were 4.0 % and 8.8 %, respectively. At the first examination, EUS was superior to other imaging modalities in terms of IPMN-derived and -concomitant PDAC detection. Throughout the study period, including follow-up, EUS was significantly better at detecting IPMN-concomitant PDACs than the other modalities. Conclusions: IPMN-concomitant PDACs are quite often found at diagnosis and during follow-up. EUS examination of the whole pancreas plays an important role in the management of IPMNs as it allows the early detection of these small invasive carcinomas.

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[70]

TÍTULO / TITLE: - Successful Treatment of Metastasized Pancreatic Vasoactive Intestinal Polypeptide-Secreting Tumor Unresponsive to High-Dose Octreotide by Peptide Receptor Radionuclide Therapy Using 90Y DOTATATE.

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

REVISTA / JOURNAL: - Clin Nucl Med. 2013 Dec;38(12):996-7. doi: 10.1097/RLU.0b013e3182a7596b.

●● Enlace al texto completo (gratuito o de pago) 1097/RLU.0b013e3182a7596b

AUTORES / AUTHORS: - Sainz-Esteban A; Baum RP

INSTITUCIÓN / INSTITUTION: - From the *Department of Nuclear Medicine, Hospital Clinico Universitario de Valladolid, Valladolid, España; and daggerTHERANOSTICS Center for Molecular Radiotherapy and Molecular Imaging, ENETS Center of Excellence, Zentralklinik Bad Berka, Bad Berka, Germany.

RESUMEN / SUMMARY: - We report a successful treatment of a patient with heavily metastasized pancreatic vasoactive intestinal polypeptide-secreting tumor, which was unresponsive to high doses of octreotide analog using peptide receptor radionuclide therapy applying a radiolabeled somatostatin analog. After the peptide receptor radionuclide therapy, there was a decrease in vasoactive intestinal polypeptide levels, a significant reduction in somatostatin receptor expression and in molecular tumor volume on Ga DOTANOC PET/CT scan, and a complete long-term resolution of symptoms of the patient.

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[71]

TÍTULO / TITLE: - Pancreatic cyst prevalence and the risk of mucin-producing adenocarcinoma in US adults.

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

REVISTA / JOURNAL: - Am J Gastroenterol. 2013 Oct;108(10):1546-50. doi: 10.1038/ajg.2013.103.

●● Enlace al texto completo (gratuito o de pago) 1038/ajg.2013.103

AUTORES / AUTHORS: - Gardner TB; Glass LM; Smith KD; Ripple GH; Barth RJ; Klibansky DA; Colacchio TA; Tsapakos MJ; Suriawinata AA; Tsongalis GJ; Pipas JM; Gordon SR

INSTITUCIÓN / INSTITUTION: - Section of Gastroenterology and Hepatology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, USA.

RESUMEN / SUMMARY: - OBJECTIVES: The presence of a pancreatic cyst often prompts concern, although the rate of malignant transformation to mucin-producing adenocarcinoma is not known. We aimed to determine the prevalence rate of mucin-producing adenocarcinoma in US adults with pancreatic cysts. METHODS: This retrospective, population-based cross-sectional study calculated the annual number of mucin-producing adenocarcinomas using the Surveillance Epidemiology and End Results (SEER 18) database and the 2010 US census. The overall prevalence rate of cysts in the population was found using data from large cross-sectional imaging studies of incidental cyst prevalence. Prevalence rates were then calculated by dividing the annual number of mucin-producing adenocarcinomas by the cyst prevalence rate. RESULTS: Between 2005 and 2009, 1,137 mucin-producing adenocarcinomas were estimated to be found annually in a US adult population of 137,154,960. The total number of pancreas cysts, given a cyst prevalence rate of 2.5%, was 3,428,874. Therefore, the prevalence rate of mucin-producing adenocarcinoma arising in patients with pancreatic cysts was 33.2 per 100,000 (95% confidence interval (CI): 21.9-44.5). The prevalence rate was 32.8 per 100,000 (95% CI: 21.6-44.0) in women and 33.5 per 100,000 (95% CI: 22.2-44.8) in men. As expected, the rate of malignant transformation increased linearly with advancing age (highest 38.6 per 100,000 in 80- to 84-year-old men). CONCLUSIONS: Malignant transformation of pancreatic cysts into mucin-producing adenocarcinoma in US adults is a very rare event. Current clinical guidelines and resource allocation for pancreatic cyst disease should be reconsidered given these findings.

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[72]

TÍTULO / TITLE: - The potential risks of pancreatitis and pancreatic cancer with GLP-1-based therapies are far outweighed by the proven and potential (cardiovascular) benefits.

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

REVISTA / JOURNAL: - Diabet Med. 2013 Oct;30(10):1148-55. doi: 10.1111/dme.12301.

●● Enlace al texto completo (gratuito o de pago) 1111/dme.12301

AUTORES / AUTHORS: - Ryder RE

INSTITUCIÓN / INSTITUTION: - Department of Diabetes and Endocrinology, City Hospital, Birmingham, UK.

RESUMEN / SUMMARY: - Recent suggestions that glucagon-like peptide-1 (GLP-1)-based therapies could cause pancreatitis, and even pancreatic cancer, are based on: ANIMAL STUDIES: The worrying histological changes are not reproduced in all studies and are unexpectedly variable with different GLP-1-based therapies. AN OBSERVATIONAL STUDY: Singh's findings that pancreatitis is doubled with GLP-1-based therapies could relate to their use in obese patients who are prone to pancreatitis risk factors—gallstones and hypertriglyceridaemia. The other observational studies do not find an association between GLP-1-based therapies and pancreatitis. US FOOD AND DRUG ADMINISTRATION ADVERSE EVENT REPORTING SYSTEM: The increased reports of pancreatitis and pancreatic cancer are likely to be attributable to 'notoriety bias'. A STUDY OF ORGAN DONOR PANCREASES: Butler's findings for those on GLP-1-based therapies vs. those not, could have other explanations. Meanwhile: META ANALYSIS: Randomized control trials with GLP-1-based therapies do not find increased pancreatitis risk. Meta-analysis of 53 randomized controlled trials including 20 212 dipeptidyl peptidase-4 inhibitor-treated patients found a significantly reduced risk of major adverse cardiovascular events [odds ratio 0.689 (0.528-0.899), P = 0.006] for dipeptidyl peptidase-4 inhibitors compared with control subjects. CARDIOVASCULAR RISK: The evidence suggests that there is more than a possibility that some of the GLP-1 receptor agonists, and possibly also some dipeptidyl peptidase-4 inhibitors, may be associated with reduced cardiovascular events. Eight ongoing long-term cardiovascular randomized controlled trials will report from September 2013 onwards. These trials should resolve the issue of pancreatitis risk and substantiate the extent of benefit. CONCLUSION: Whilst we should remain vigilant, currently the balance of evidence is strongly in support of GLP-1-based therapy, with benefits far outweighing potential risks.

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[73]

TÍTULO / TITLE: - Transluminal endoscopic step-up approach versus minimally invasive surgical step-up approach in patients with infected necrotising pancreatitis (TENSION trial): design and rationale of a randomised controlled multicenter trial [ISRCTN09186711].

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

REVISTA / JOURNAL: - BMC Gastroenterol. 2013 Nov 25;13(1):161.

●● Enlace al texto completo (gratuito o de pago) 1186/1471-230X-13-161

AUTORES / AUTHORS: - van Brunschot S; van Grinsven J; Voermans RP; Bakker OJ; Besselink MG; Boermeester MA; Bollen TL; Bosscha K; Bouwense SA; Bruno MJ; Cappendijk VC; Consten EC; Dejong CH; Dijkgraaf MG; van Eijck CH; Erkelens GW;

van Goor H; Hadithi M; Haveman JW; Hofker SH; Jansen JJ; Lameris JS; van Lienden KP; Manusama ER; Meijssen MA; Mulder CJ; Nieuwenhuis VB; Poley JW; de Ridder RJ; Rosman C; Schaapherder AF; Scheepers JJ; Schoon EJ; Seerden T; Spanier BM; Straathof JW; Timmer R; Venneman NG; Vleggaar FP; Witteman BJ; Gooszen HG; van Santvoort HC; Fockens P

RESUMEN / SUMMARY: - BACKGROUND: Infected necrotising pancreatitis is a potentially lethal disease that nearly always requires intervention. Traditionally, primary open necrosectomy has been the treatment of choice. In recent years, the surgical step-up approach, consisting of percutaneous catheter drainage followed, if necessary, by (minimally invasive) surgical necrosectomy has become the standard of care. A promising minimally invasive alternative is the endoscopic transluminal step-up approach. This approach consists of endoscopic transluminal drainage followed, if necessary, by endoscopic transluminal necrosectomy. We hypothesise that the less invasive endoscopic step-up approach is superior to the surgical step-up approach in terms of clinical and economic outcomes.Methods/design: The TENSION trial is a randomised controlled, parallel-group superiority multicenter trial. Patients with (suspected) infected necrotising pancreatitis with an indication for intervention and in whom both treatment modalities are deemed possible, will be randomised to either an endoscopic transluminal or a surgical step-up approach. During a 4 year study period, 98 patients will be enrolled from 24 hospitals of the Dutch Pancreatitis Study Group. The primary endpoint is a composite of death and major complications within 6 months following randomisation. Secondary endpoints include complications such as pancreaticocutaneous fistula, exocrine or endocrine pancreatic insufficiency, need for additional radiological, endoscopic or surgical intervention, the need for necrosectomy after drainage, the number of (re-)interventions, quality of life, and total direct and indirect costs. DISCUSSION: The TENSION trial will answer the question whether an endoscopic step-up approach reduces the combined primary endpoint of death and major complications, as well as hospital stay and related costs compared with a surgical step-up approach in patients with infected necrotising pancreatitis.

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[74]

TÍTULO / TITLE: - Cellular and plasma uptake of parenteral omega-3 rich lipid emulsion fatty acids in patients with advanced pancreatic cancer.

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

REVISTA / JOURNAL: - Clin Nutr. 2013 Oct 6. pii: S0261-5614(13)00257-4. doi: 10.1016/j.clnu.2013.09.017.

●● Enlace al texto completo (gratuito o de pago) 1016/j.clnu.2013.09.017

AUTORES / AUTHORS: - Arshad A; Chung WY; Isherwood J; Mann CD; Al-Leswas D; Steward WP; Metcalfe MS; Dennison AR

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary and Pancreatic Surgery, Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW, UK. Electronic address: ali.arshad@doctors.org.uk.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Omega-3 rich fatty acids (n-3FA) have powerful anti-inflammatory and anti-neoplastic properties. Previous studies have investigated plasma and cellular uptake of oral and parenteral n-3FA regimens. These have shown that n-3FA undergo rapid uptake into cells which is sustained for the length of the treatment course. The aim of this study was to investigate long-term

uptake of prolonged, regular treatment courses of parenteral n-3FA which has not been previously reported. METHODS: As part of a phase II single-arm trial, patients with advanced pancreatic cancer were treated with gemcitabine plus parenteral n-3FA rich lipid emulsion (up to 100 g) each week for three consecutive weeks with a subsequent rest week. This was repeated for up to six months in total for each patient. Pre-treatment serum and erythrocyte cell membrane (ECM) pellet samples were obtained each week for the entire treatment course of each patient. Post-treatment samples were obtained for the first two cycles only to assess rapid uptake. Fatty acid methyl esters (FAME) were produced and analysed using gas chromatography. FAME proportions as a total of sample lipid composition for each class were plotted and the results analysed using a linear regression coefficient model. RESULTS: There was rapid and significant uptake of EPA and DHA FAME into plasma Non-Esterified Fatty Acids (NEFA) and EPA into ECM pellets in post-treatment samples (median increase of 1.06%, 0.65% and 0.05% respectively). There was significant reduction in n-6 fatty acid FAMEs and DHA in ECM pellets (decrease of 0.31% and 0.8% respectively- p = 0.031 for all). There was significant sustained uptake of EPA and DHA FAME into ECM pellets over the cohort's pooled treatment course with corresponding reduction in the n-6:n-3 ratio. CONCLUSIONS: Prolonged regular parenteral n-3FA administration results in rapid and sustained cellular uptake. This regimen is appropriate for therapies aimed at increasing n-3FA content of cellular membranes and reduction of the n-6:n-3 ratio.

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[75]

TÍTULO / TITLE: - Novel insights into pancreatic beta-cell glucolipotoxicity from real-time functional analysis of mitochondrial energy metabolism in INS-1E insulinoma cells.

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

REVISTA / JOURNAL: - Biochem J. 2013 Dec 15;456(3):417-26. doi: 10.1042/BJ20131002.

●● Enlace al texto completo (gratuito o de pago) 1042/BJ20131002

AUTORES / AUTHORS: - Barlow J; Affourtit C

INSTITUCIÓN / INSTITUTION: - *School of Biomedical and Healthcare Sciences, Plymouth University, Drake Circus, Plymouth PL4 8AA, U.K.

RESUMEN / SUMMARY: - High circulating glucose and non-esterified (free) fatty acid levels can cause pancreatic beta-cell failure. The molecular mechanisms of this beta-cell glucolipotoxicity are yet to be established conclusively. In the present paper we report on the involvement of mitochondrial dysfunction in fatty-acid-induced beta-cell failure. We have used state-of-the-art extracellular flux technology to functionally probe mitochondrial energy metabolism in intact INS-1E insulinoma cells in real-time. We show that 24-h palmitate exposure at high glucose attenuates the glucose-sensitivity of mitochondrial respiration and lowers coupling efficiency of glucose-stimulated oxidative phosphorylation. These mitochondrial defects coincide with an increased level of ROS (reactive oxygen species), impaired GSIS (glucose-stimulated insulin secretion) and decreased cell viability. Palmitate lowers absolute glucose-stimulated respiration coupled to ATP synthesis, but does not affect mitochondrial proton leak. Palmitate is not toxic when administered at low glucose unless fatty acid beta-oxidation is inhibited. Palmitoleate, on the other hand, does not affect mitochondrial respiration, ROS levels, GSIS or cell viability. Although palmitoleate protects against the palmitate-induced

ROS increase and cell viability loss, it does not protect against respiratory and insulin secretory defects. We conclude that mitochondrial dysfunction contributes to fatty-acid-induced GSIS impairment, and that glucolipotoxic cell viability and GSIS phenotypes are mechanistically distinct.

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[76]
TÍTULO / TITLE: - Risk of pancreatic cancer among individuals with hepatitis C or hepatitis B virus infection: a nationwide study in Sweden.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 26;109(11):2917-23. doi: 10.1038/bjc.2013.689. Epub 2013 Oct 31.
●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.689
AUTORES / AUTHORS: - Huang J; Magnusson M; Torner A; Ye W; Duberg AS
INSTITUCIÓN / INSTITUTION: - Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, 171 77 Stockholm, Sweden.
RESUMEN / SUMMARY: - Background:A few studies indicated that hepatitis C and hepatitis B virus (HCV/HBV) might be associated with pancreatic cancer risk. The aim of this nationwide cohort study was to examine this possible association.Methods:Hepatitis C virus- and hepatitis B virus-infected individuals were identified from the national surveillance database from 1990 to 2006, and followed to the end of 2008. The pancreatic cancer risk in the study population was compared with the general population by calculation of Standardized Incidence Ratios (SIRs), and with a matched reference population using a Cox proportional hazards regression model to calculate hazard ratios (HRs).Results:In total 340 819 person-years in the HCV cohort and 102 295 in the HBV cohort were accumulated, with 34 and 5 pancreatic cancers identified, respectively. The SIRHCV was 2.1 (95% confidence interval, CI: 1.4, 2.9) and the SIRHBV was 1.4 (0.5, 3.3). In the Cox model analysis, the HR for HCV infection was 1.9 (95% CI: 1.3, 2.7), diminishing to 1.6 (1.04, 2.4) after adjustment for potential confounders.Conclusion:Our results indicated that HCV infection might be associated with an increased risk of pancreatic cancer but further studies are needed to verify such association. The results in the HBV cohort indicated an excess risk, however, without statistical significance due to lack of power.

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[77]
TÍTULO / TITLE: - MiR-365 induces gemcitabine resistance in pancreatic cancer cells by targeting the adaptor protein SHC1 and pro-apoptotic regulator BAX.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cell Signal. 2013 Nov 9;26(2):179-185. doi: 10.1016/j.cellsig.2013.11.003.
●● Enlace al texto completo (gratuito o de pago) 1016/j.cellsig.2013.11.003
AUTORES / AUTHORS: - Hamada S; Masamune A; Miura S; Satoh K; Shimosegawa T
INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology, Tohoku University Graduate School of Medicine, 1-1, Seiryo-machi, Aobaku, Sendai City, Miyagi 980-8574, Japan. Electronic address: hamadas@med.tohoku.ac.jp.
RESUMEN / SUMMARY: - The poor prognosis of invasive ductal adenocarcinoma of the pancreas is mainly due to its resistance against therapeutic agents. The molecular

mechanism by which morbidity enhances cell survival has been extensively studied, but radical improvements in the therapeutic strategy have not yet been achieved. Recent reports have indicated the substantial contribution of miRNA in multiple cell functions by comprehensively targeting clusters of genes. We identified several miRNAs highly expressed in invasive ductal adenocarcinoma in our previous study, and clarified their contribution to the epithelial-mesenchymal transition. Among the differentially expressed miRNAs, miR-365 was highly expressed in invasive ductal adenocarcinoma, whose functional role has not been reported. In the current study, we found that miR-365 induced gemcitabine resistance in pancreatic cancer cells. MiR-365 directly targeted adaptor protein Src Homology 2 Domain Containing 1 (SHC1) and apoptosis-promoting protein BAX. The siRNA-based knockdown of SHC1 and BAX increased gemcitabine resistance, indicating the miR-365/SHC1/BAX axis influences the survival of pancreatic cancer cells. In addition, miR-365 up-regulated cancer-promoting molecules such as Inhibitor of DNA binding 2 and S100P, suggesting the existence of cross-talk with other cancer-promoting signals. MiR-365 could exert orchestrated effects on pancreatic cancer cell survival.

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[78]

TÍTULO / TITLE: - MUC4-mediated regulation of acute phase protein lipocalin 2 through HER2/AKT/NF-kappaB signaling in pancreatic cancer.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 15.

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-2174

AUTORES / AUTHORS: - Kaur S; Sharma N; Krishn SR; Lakshmanan I; Baine MJ; Rachagani S; Smith L; Lele SM; Sasson AR; Guha S; Anderson JM; Mallya K; Hollingsworth MT; Batra SK

INSTITUCIÓN / INSTITUTION: - Biochemistry and Molecular Biology, University of Nebraska Medical Center.

RESUMEN / SUMMARY: - PURPOSE: MUC4 shows aberrant expression in early pancreatic lesions and a high specificity for pancreatic cancer (PC). It thus has a high potential to be a sensitive and specific biomarker. Unfortunately, its low serum level limits its diagnostic/prognostic potential. We here report that a multi-faceted acute phase protein lipocalin 2, regulated by MUC4, could be a potential diagnostic/prognostic marker for pancreatic cancer. Experimental Designs and RESULTS: Overexpression/knockdown, luciferase reporter and molecular inhibition studies revealed that MUC4 regulates lipocalin 2 by stabilizing HER2 and stimulating AKT, which results in the activation of NF-kappaB. Immunohistochemical analyses of lipocalin 2 and MUC4 showed a significant positive correlation between MUC4 and lipocalin 2 in primary, metastatic tissues (Spearman correlation coefficient 0.71, p-value=0.002) from rapid autopsy tissue sample from PC patients as well as in serum and tissue samples from spontaneous KRASG12D mouse PC model (Spearman correlation coefficient 0.98, p-value <0.05). Lipocalin 2 levels increased progressively with disease advancement (344.2 +/-22.8 ng/ml for 10 week to 3067.2+/-572.6 for 50 week; p<0.0001). In human PC cases, significantly elevated levels of lipocalin 2 were observed in PC patients (148+/-13.18 ng/ml) in comparison to controls (73.27+/-4.9 ng/ml, p-value=0.014). Analyses of pre- and post-chemotherapy patients showed

higher lipocalin 2 levels in pre-chemotherapy patients (121.7 ng/ml, 95% C.I. 98.1-150.9) in comparison to the post-chemotherapy (92.6 ng/ml, 95% C.I. 76.7-111.6, p-value=0.06) group. CONCLUSIONS: The present study delineates the association and the downstream mechanisms of MUC4-regulated elevation of lipocalin-2 (via HER2/AKT/NF-kappaB) and its clinical significance for prognosis of pancreatic cancer.

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[79]

TÍTULO / TITLE: - Preclinical validation of AXL receptor as a target for antibody-based pancreatic cancer immunotherapy.

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

REVISTA / JOURNAL: - Oncogene. 2013 Nov 18. doi: 10.1038/onc.2013.487.

●● Enlace al texto completo (gratuito o de pago) 1038/onc.2013.487

AUTORES / AUTHORS: - Leconet W; Larbouret C; Chardes T; Thomas G; Neiveyans M; Busson M; Jarlier M; Radosevic-Robin N; Pugniere M; Bernex F; Penault-Llorca F; Pasquet JM; Pelegrin A; Robert B

INSTITUCIÓN / INSTITUTION: - INSERM-U896, IRCM, Universite Montpellier1, CRLC Val d'Aurelle-Paul Lamarque, 208 rue des Apothicaires, Montpellier-Cedex 5, France.

RESUMEN / SUMMARY: - AXL receptor tyrosine kinase (RTK) is implicated in proliferation and invasion of many cancers, particularly in pancreatic ductal adenocarcinoma (PDAC), for which new therapeutic options are urgently required. We investigated whether inhibition of AXL activity by specific monoclonal antibodies (mAbs) is efficient in limiting proliferation and migration of pancreatic cancer cells. Expression of AXL was evaluated by immunohistochemistry in 42 PDAC. The AXL role in oncogenesis was studied using the short hairpin RNA approach in a pancreatic carcinoma cell line. We further generated antihuman AXL mAbs and evaluated their inhibitory effects and the AXL downstream signaling pathways first in vitro, in a panel of pancreatic cancer cell lines and then in vivo, using subcutaneous or orthotopic pancreatic tumor xenografts. AXL receptor was found expressed in 76% (32/42) of PDAC and was predominantly present in invasive cells. The AXL-knockdown Panc-1 cells decreased in vitro cell migration, survival and proliferation, and reduced in vivo tumor growth. Two selected anti-AXL mAbs (D9 and E8), which inhibited phosphorylation of AXL and of its downstream target AKT without affecting growth arrest-specific factor 6 (GAS6) binding, induced downexpression of AXL by internalization, leading to an inhibition of proliferation and migration in the four pancreatic cancer cell lines studied. In vivo, treatment by anti-AXL mAbs significantly reduced growth of both subcutaneous and orthotopic pancreatic tumor xenografts independently of their KRAS mutation status. Our in vitro and preclinical in vivo data demonstrate that anti-human AXL mAbs could represent a new approach to the pancreatic cancer immunotherapy.Oncogene advance online publication, 18 November 2013; doi:10.1038/onc.2013.487.

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[80]

TÍTULO / TITLE: - Hypercalcemia associated with adenosquamous pancreatic carcinoma: A reason to initiate palliative treatment.

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

REVISTA / JOURNAL: - Rev Esp Enferm Dig. 2013 Aug;105(7):425-428.

AUTORES / AUTHORS: - Lopez-Tomassetti-Fernandez EM; Favre-Rizzo J; Delgado-Plasencia L; Hernandez-Hernandez JR

RESUMEN / SUMMARY: - Background: hypercalcemia in patients with diagnosed carcinoma has predominantly a humoral basis mediated by parathyroid hormone-related protein (PTH-rP). Among the reported cases, hypercalcemia associated with the majority of abdominal malignancies indicates an advanced stage of disease.Case report: we present a case of a 78-year-old patient with an adenosquamous pancreatic carcinoma associated with humoral hypercalcemia mediated by PTH-rP.Conclusion: in this case, demonstration of unexpectantly rapid increase in calcium serum correlated with aggressive tumor growth led us to raise the hypothesis that PTH-rP could be a mediator of invasion and dissemination secreted by some tumors, and probably indicates the appropriate time to initiate palliative treatment.

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[81]

TÍTULO / TITLE: - Management of Renal Masses in Transplant Allografts at an Australian Kidney-Pancreas Transplant Unit.

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

REVISTA / JOURNAL: - Transplantation. 2013 Nov 7.

●● Enlace al texto completo (gratuito o de pago)

1097/01.TP.0000437333.38786.fd

AUTORES / AUTHORS: - Su MZ; Campbell NA; Lau HM

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RESUMEN / SUMMARY: - BACKGROUND: A shift towards partial nephrectomy (PN) in the management of small renal cell carcinoma (RCC) in recent years has prompted a parallel change in the management of rare cases of transplant allograft RCC. There are currently no guidelines on the management of allograft RCC. We present our center experience and review the latest evidence for management of RCC in renal transplant allografts. METHODS: We performed a retrospective review of the transplant patient registry of a kidney-pancreas transplant center between 1984 and 2012. All confirmed allograft kidney RCC cases were included in this series. MEDLINE search of current literature on renal allograft RCC and selection of appropriate studies were conducted. RESULTS: A total of 1,241 patients had received either a living, cadaveric, or combined kidney-pancreas transplant at our center, and four cases of allograft RCC were identified. The first case underwent a radical nephrectomy given the central location of the tumor and his young age. The second case underwent an open PN in the setting of a central tumor with minimal morbidity. The third case involved multiple renal lesions that were subsequently treated with radiofrequency ablation (RFA). The fourth case underwent a non-ischemic open PN in the setting of a midpole tumor with minimal morbidity. There have been no cases of local recurrence or metastatic progression at median 21.5 months' follow-up. CONCLUSION: We have shown the safety and efficacy of minimally invasive techniques such as PN and RFA in a variety of tumors. We consider PN as an appropriate therapy for localized, clinical T1 allograft RCC tumors.

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[82]

TÍTULO / TITLE: - Nut consumption and risk of pancreatic cancer in women.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 26;109(11):2911-6. doi: 10.1038/bjc.2013.665. Epub 2013 Oct 22.

●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.665

AUTORES / AUTHORS: - Bao Y; Hu FB; Giovannucci EL; Wolpin BM; Stampfer MJ; Willett WC; Fuchs CS

INSTITUCIÓN / INSTITUTION: - Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, 181 Longwood Avenue, Boston, MA 02115, USA.

RESUMEN / SUMMARY: - Background:Increasing nut intake has been associated with reduced risk of diabetes mellitus, which is a risk factor for pancreatic cancer.Methods:We prospectively followed 75 680 women in the Nurses' Health Study, and examined the association between nut consumption and pancreatic cancer risk. Participants with a previous history of cancer were excluded. Nut consumption was assessed at baseline and updated every 2 to 4 years. Relative risks (RRs) and 95% confidence intervals (95% CIs) were estimated using Cox proportional hazards models.Results:We documented 466 incident cases of pancreatic cancer. After adjusting for age, height, smoking, physical activity, and total energy intake, women who consumed a 28-g (1 oz) serving size of nuts >/=2 times per week experienced a significantly lower risk of pancreatic cancer (RR, 0.65; 95% CI, 0.47-0.92; P for trend=0.007) when compared with those who largely abstained from nuts. The results did not appreciably change after further adjustment for body mass index (BMI) and history of diabetes mellitus (RR, 0.68; 95% CI, 0.48-0.95; P for trend=0.01). The inverse association persisted within strata defined by BMI, physical activity, smoking, and intakes of red meat, fruits, and vegetables.Conclusion:Frequent nut consumption is inversely associated with risk of pancreatic cancer in this large prospective cohort of women, independent of other potential risk factors for pancreatic cancer.

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[83]

TÍTULO / TITLE: - Predictive value of maximum standardized uptake value (SUVmax) on 18F-FDG PET/CT in patients with locally advanced or metastatic pancreatic cancer.

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

REVISTA / JOURNAL: - Clin Nucl Med. 2013 Oct;38(10):778-83. doi: 10.1097/RLU.0b013e31829f8c90.

●● Enlace al texto completo (gratuito o de pago) 1097/RLU.0b013e31829f8c90

AUTORES / AUTHORS: - Moon SY; Joo KR; So YR; Lim JU; Cha JM; Shin HP; Yang YJ

INSTITUCIÓN / INSTITUTION: - From the *Departments of Gastroenterology and daggerNuclear Medicine, Kyung Hee University School of Medicine, Kyung Hee University Hospital at Gangdong, Seoul, Republic of Korea.

RESUMEN / SUMMARY: - PURPOSE: We investigated the prognostic role of 18F-FDG PET/CT in the prediction of progression-free survival (PFS) and chemotherapeutic response in patients with locally advanced or metastatic pancreatic cancer.

METHODS: We enrolled 21 newly diagnosed patients with locally advanced or metastatic pancreatic cancer who underwent 18F-FDG PET/CT scanning before palliative gemcitabine-based chemotherapy between 2006 and 2012. Maximum standardized uptake value (SUVmax) of the primary tumor was measured by 18F-FDG PET/CT. Chemotherapeutic response was evaluated according to the Response Evaluation Criteria in Solid Tumors. Survival analysis was performed for time to progression using the Kaplan-Meier method. Cox proportional hazard models were used to determine independent prognostic factors. RESULTS: All pancreatic tumors showed detectable FDG uptake (mean SUVmax = 6.8 +/- 3.0, range 2-12) The mean SUVmax values among response groups showed no significant difference (P = 0.853) and chemotherapeutic response was not different according to SUVmax level (P = 0.807). PFS was significantly shorter in the high SUVmax (>/=6.8) group than in the low SUVmax (<6.8) group (2.9 vs. 6 months, P = 0.012). Multivariate analysis revealed that SUVmax was an independent prognostic factor for predicting PFS (P = 0.046). CONCLUSIONS: Higher SUVmax of primary pancreatic tumor is associated with poor PFS and pretreatment SUVmax is an independent prognostic factor for predicting PFS in patients with locally advanced or metastatic pancreatic cancer who received gemcitabine-based palliative chemotherapy. However, pretreatment SUVmax is not associated with chemotherapeutic response.

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[84]

TÍTULO / TITLE: - Synergistic interaction of novel lactate dehydrogenase inhibitors with gemcitabine against pancreatic cancer cells in hypoxia.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Oct 31. doi: 10.1038/bjc.2013.681.

●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.681

AUTORES / AUTHORS: - Maftouh M; Avan A; Sciarrillo R; Granchi C; Leon LG; Rani R; Funel N; Smid K; Honeywell R; Boggi U; Minutolo F; Peters GJ; Giovannetti E

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, VU University Medical Center, De Boelelaan 1117, 1081HV, Amsterdam, Netherlands.

RESUMEN / SUMMARY: - Background:Hypoxia is a driving force in pancreatic-ductal-adenocarcinoma (PDAC) growth, metastasis and chemoresistance. The muscle-isoform of lactate dehydrogenase (LDH-A) constitutes a major checkpoint for the switch to anaerobic glycolysis, ensuring supply of energy and anabolites in hypoxic-environments. Therefore, we investigated the molecular mechanisms underlying the pharmacological interaction of novel LDH-A inhibitors in combination with gemcitabine in PDAC cells.Methods:Lactate dehydrogenase A levels were studied by quantitative RT-PCR, western blot, immunofluorescence and activity assays in 14 PDAC cells, including primary-cell-cultures and spheroids, in normoxic and hypoxic conditions. Cell proliferation, migration and key determinants of drug activity were evaluated by sulforhodamine-B-assay, wound-healing assay, PCR and LC-MS/MS.Results:Lactate dehydrogenase A was significantly increased under hypoxic conditions (1% O2), where the novel LDH-A inhibitors proved to be particularly effective (e.g., with IC50 values of 0.9 vs 16.3 muM for NHI-1 in LPC006 in hypoxia vs normoxia, respectively). These compounds induced apoptosis, affected invasiveness and spheroid-growth, reducing expression of metalloproteinases and cancer-stem-like-cells markers (CD133+). Their synergistic interaction with gemcitabine, with combination index values <0.4 in hypoxia,

might also be attributed to modulation of gemcitabine metabolism, overcoming the reduced synthesis of phosphorylated metabolites.Conclusion:Lactate dehydrogenase A is a viable target in PDAC, and novel LDH-A inhibitors display synergistic cytotoxic activity with gemcitabine, offering an innovative tool in hypoxic tumours.British Journal of Cancer advance online publication, 31 October 2013; doi:10.1038/bjc.2013.681 www.bjcancer.com.

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[85]

TÍTULO / TITLE: - microRNA-10b enhances pancreatic cancer cell invasion by suppressing TIP30 expression and promoting EGF and TGF-beta actions.

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

REVISTA / JOURNAL: - Oncogene. 2013 Oct 7. doi: 10.1038/onc.2013.405.

●● Enlace al texto completo (gratuito o de pago) 1038/onc.2013.405

AUTORES / AUTHORS: - Ouyang H; Gore J; Deitz S; Korc M

INSTITUCIÓN / INSTITUTION: - Departments of Medicine, Biochemistry and Molecular Biology, Indiana University School of Medicine, the Melvin and Bren Simon Cancer Center and the Pancreatic Cancer Signature Center, Indianapolis, IN, USA.

RESUMEN / SUMMARY: - Increased microRNA-10b (miR-10b) expression in the cancer cells in pancreatic ductal adenocarcinoma (PDAC) is a marker of disease aggressiveness. In the present study, we determined that plasma miR-10b levels are significantly increased in PDAC patients by comparison with normal controls. By gene profiling, we identified potential targets downregulated by miR-10b, including Tat-interacting protein 30 (TIP30). Immunoblotting and luciferase reporter assays confirmed that TIP30 was a direct miR-10b target. Downregulation of TIP30 by miR-10b or siRNA-mediated silencing of TIP30 enhanced epidermal growth factor (EGF)-dependent invasion. The actions of miR-10b were abrogated by expressing a modified TIP30 cDNA resistant to miR-10b. EGF-induced EGF receptor (EGFR) tyrosine phosphorylation and extracellular signal-regulated kinase phosphorylation were enhanced by miR-10b, and these effects were mimicked by TIP30 silencing. The actions of EGF in the presence of miR-10b were blocked by EGFR kinase inhibition with erlotinib and by dual inhibition of PI3K (phosphatidylinositol 3'-kinase) and MEK. Moreover, miR-10b, EGF and transforming growth factor-beta (TGF-beta) combined to markedly increase cell invasion, and this effect was blocked by the combination of erlotinib and SB505124, a type I TGF-beta receptor inhibitor. miR-10b also enhanced the stimulatory effects of EGF and TGF-beta on cell migration and epithelial-mesenchymal transition (EMT) and decreased the expression of RAP2A, EPHB2, KLF4 and NF1. Moreover, miR-10b overexpression accelerated pancreatic cancer cell (PCC) proliferation and tumor growth in an orthotopic model. Thus, plasma miR-10b levels may serve as a diagnostic marker in PDAC, whereas intra-tumoral miR-10b promotes PCC proliferation and invasion by suppressing TIP30, which enhances EGFR signaling, facilitates EGF-TGF-beta cross-talk and enhances the expression of EMT-promoting genes, whereas decreasing the expression of several metastasis-suppressing genes. Therefore, therapeutic targeting of miR-10b in PDAC may interrupt growth-promoting deleterious EGF-TGF-beta interactions and antagonize the metastatic process at various levels.Oncogene advance online publication, 7 October 2013; doi:10.1038/onc.2013.405.

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[86]

TÍTULO / TITLE: - Effectivity of Long Antigen Exposition Dendritic Cell Therapy (LANEXDC®) in the Palliative Treatment of Pancreatic Cancer.

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

REVISTA / JOURNAL: - Curr Med Chem. 2013;20(38):4827-35.

AUTORES / AUTHORS: - Gansauge F; Poch B; Kleef R; Schwarz M

INSTITUCIÓN / INSTITUTION: - Center for oncologic, endocrine and minimal-invasive surgery, Silcherstr. 36, 89231 Neu-Ulm, Germany. frank.gansauge@eurosurgery.de.

RESUMEN / SUMMARY: - Purpose: In pancreatic cancer median survival times range around 6, 6 to 6,9 months. Here we retrospectively analyzed the outcome of immunotherapy in the additional palliative treatment of pancreatic cancer with long antigen exposition dendritic cell therapy (LANEX-DC(®)) in 138 patients who were treated at our institution. Patients: Data were available of 134 patients (97.1%). The median interval between first diagnosis and start of treatment was 1.4 months. Results: Therapy was well tolerated and no serious side effects were observed. The survival rate after 6 months was 72.2 % and afters 9 month 50.4%. The median survival time according to Kaplan- Meier regression analysis was 8.9 months. Median survival was significantly higher in the group of patients who started immunotherapy within 2 months following diagnosis (p=0.029) or repeated immunotherapy (p=0.027). Interestingly, younger patients <= 60 years of age lived significantly longer as patients > 60 years of age (p = 0.022). Conclusion: We were able to demonstrate in a large retrospective analysis that additional treatment with dendritic cells (LANEX-DC(®)) is highly effective and extends the median survival times up to 8.9 months. Furthermore we were able to demonstrate that median survival can be increased by early beginning and repetition of LANEX-DC(®) treatment.

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[87]

TÍTULO / TITLE: - Phase I study of neoadjuvant accelerated short course radiation therapy with photons and capecitabine for resectable pancreatic cancer.

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

REVISTA / JOURNAL: - Radiother Oncol. 2013 Nov 11. pii: S0167-8140(13)00536-7. doi: 10.1016/j.radonc.2013.10.027.

●● Enlace al texto completo (gratuito o de pago) 1016/j.radonc.2013.10.027

AUTORES / AUTHORS: - Wo JY; Mamon HJ; Ferrone CR; Ryan DP; Blaszkowsky LS; Kwak EL; Tseng YD; Napolitano BN; Ancukiewicz M; Swanson RS; Lillemoe KD; Castillo CF; Hong TS

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, United States. Electronic address: jwo@partners.org.

RESUMEN / SUMMARY: - PURPOSE: In this phase I study, we sought to determine the feasibility and tolerability of neoadjuvant short course radiotherapy (SC-CRT) delivered with photon RT with concurrent capecitabine for resectable pancreatic adenocarcinoma. MATERIALS AND METHODS: Ten patients with localized, resectable pancreatic adenocarcinoma were enrolled from December 2009 to August 2011. In dose level I, patients received 3Gyx10. In dose level 2, patients received 5Gyx5 (every other day). In dose level 3, patients received 5Gyx5 (consecutive days).

Capecitabine was given during weeks 1 and 2. Surgery was performed 1-3weeks after completion of chemotherapy. RESULTS: With an intended accrual of 12 patients, the study was closed early due to unexpected intraoperative complications. Compared to the companion phase I proton study, patients treated with photons had increased intraoperative RT fibrosis reported by surgeons (27% vs. 63%). Among those undergoing a Whipple resection, increased RT fibrosis translated to an increased mean OR time of 69min. Dosimetric comparison revealed significantly increased low dose exposure to organs at risk for patients treated with photon RT. CONCLUSIONS: This phase I experience evaluating the tolerability of neoadjuvant SC-CRT with photon RT closed early due to unexpected intraoperative complications.

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[88]

TÍTULO / TITLE: - Seropositivity to Helicobacter pylori and Risk of Pancreatic Cancer.

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

REVISTA / JOURNAL: - Cancer Epidemiol Biomarkers Prev. 2013 Nov 27.

●● Enlace al texto completo (gratuito o de pago) 1158/1055-9965.EPI-13-0680

AUTORES / AUTHORS: - Yu G; Murphy G; Michel A; Weinstein SJ; Mannisto S; Albanes D; Pawlita M; Stolzenberg-Solomon RZ

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, Bethesda, Maryland; Division of Genome Modifications and Carcinogenesis, Research Program Infection and Cancer, German Cancer Research Center, Heidelberg, Germany; and Department of Chronic Disease Prevention, National Institute for Health and Welfare, Helsinki, Finland.

RESUMEN / SUMMARY: - Helicobacter pylori (H. pylori) seropositivity has been inconsistently associated with pancreatic cancer. We, therefore, investigated the association between H. pylori seropositivity and pancreatic cancer in a case-control study nested within Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC) cohort of Finnish male smokers. Pancreatic cancer cases (n = 353) and control subjects (n = 353) were matched on date of baseline serum collection, age at randomization, and follow-up time (up to 23.9 years). We used a multiplex serology assay to determine the sero-status of antibodies against 15 H. pylori-specific antigens in fasting serum samples. Conditional logistic regression was used to calculate the odds ratio (OR) and 95% confidence intervals (CI). Neither targeted H. pylori antigens in serum nor the combination of all was associated with development of pancreatic cancer (combination of all: OR, 0.85; 95% CI, 0.49-1.49). Our results suggest that H. pylori is not a risk factor for pancreatic cancer. Cancer Epidemiol Biomarkers Prev; 22(12); 1-4. ©2013 AACR.

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[89]

TÍTULO / TITLE: - Helicobacter pylori Seropositivities and Risk of Pancreatic Carcinoma.

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

REVISTA / JOURNAL: - Cancer Epidemiol Biomarkers Prev. 2013 Nov 14.

●● Enlace al texto completo (gratuito o de pago) 1158/1055-9965.EPI-13-0447

AUTORES / AUTHORS: - Risch HA; Lu L; Kidd MS; Wang J; Zhang W; Ni Q; Gao YT; Yu H

INSTITUCIÓN / INSTITUTION: - Dept of Chronic Disease Epidemiology, Yale University School of Public Health.

RESUMEN / SUMMARY: - BACKGROUND: Pathophysiologic actions of Helicobacter pylori colonization on gastric acidity have been hypothesized to modulate the effect of pancreatic carcinogens, through CagA-negative organism strain type, hyperchlorhydria and increased risk of pancreatic cancer, or CagA-positive strain, hypochlorhydria and decreased risk of pancreatic cancer. We aimed to determine H. pylori strain-specific associations with pancreatic cancer in a population where colonization by CagA-positive strains is common. METHODS: We carried out a large population-based case-control study of pancreatic carcinoma in Shanghai, China. Venipuncture specimens were obtained from a representative sample of 761 case patients and 794 randomly selected control subjects matched by category of age and gender. Antibody seropositivity for H. pylori and its virulence protein CagA were determined by commercial enzyme-linked immunosorbent IgG assays. RESULTS: Compared to individuals seronegative for both H. pylori and CagA, decreased pancreas-cancer risk was seen for CagA seropositivity (adjusted odds ratio [OR], 0.68; 95% confidence interval (CI), 0.54-0.84), while some increased risk was suggested for CagA-negative H. pylori seropositivity (OR, 1.28; 95% CI, 0.76-2.13). No risk interactions were observed between CagA seropositivity and gender, cigarette smoking, or age-21 body mass index. CONCLUSIONS: Similar to what has been seen in animal models, our results provide suggestive evidence in humans for the involvement of gastric acidity, through its bidirectional modification according to colonization by Helicobacter pylori CagA strain type, in the risk of pancreatic carcinoma. IMPACT: Helicobacter pylori colonization may have diverse effects on cancer risk, depending on the organism strain type as well as on the particular cancer site.

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[90]

TÍTULO / TITLE: - High Expression of Interleukin-22 and Its Receptor Predicts Poor Prognosis in Pancreatic Ductal Adenocarcinoma.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Oct 17.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3322-x

AUTORES / AUTHORS: - Wen Z; Liao Q; Zhao J; Hu Y; You L; Lu Z; Jia C; Wei Y; Zhao Y

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Tsinghua University, Beijing, China.

RESUMEN / SUMMARY: - BACKGROUND: The cytokine interleukin-22 (IL-22) and its receptor are present in the tumor microenvironment. Their function in pancreatic ductal adenocarcinoma (PDAC) remains largely unknown. The goal of the present study was to measure the expression of IL-22 and IL-22R in PDAC and assess their relationship with clinicopathological features and prognosis. METHODS: The expression of IL-22 and IL-22R was evaluated by immunohistochemistry in PDAC tissues from 57 patients and by Western blotting in six tumors and adjacent nontumor tissues. A statistical analysis was conducted to assess the relationship between levels of expression, clinicopathological factors, and overall survival. In addition, the relationship between the expression of IL-22 and IL-22R and invasion was assessed by Western blotting and

transwell assay with the PDAC cell lines PANC1 and BxPC3. RESULTS: Positive IL-22 staining was detected in PDAC tissues and adjacent nontumor tissues. Positive IL-22R staining was detected in PDAC cells. High expression of IL-22 and IL-22R correlated significantly with lymph node involvement. IL-22 increased the phosphorylation of signal transducer and activator of transcription3, the expression of matrix metalloproteinase 9, and the invasion in PANC1 and BxPC3 cells in vitro while silencing of IL-22R RNA caused opposite effects. Most importantly, overall survival was significantly poorer in patients with high expression of IL-22 and IL-22R than in those with low expression. CONCLUSIONS: These findings reveal the positive role of IL-22 and IL-22R in invasion and metastasis in human PDAC. IL-22 and IL-22R may be suitable independent prognostic markers in PDAC.

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[91]

TÍTULO / TITLE: - Cyclic AMP regulates the migration and invasion potential of human pancreatic cancer cells.

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

REVISTA / JOURNAL: - Mol Carcinog. 2013 Sep 24. doi: 10.1002/mc.22091.

●● Enlace al texto completo (gratuito o de pago) 1002/mc.22091

AUTORES / AUTHORS: - Zimmerman NP; Roy I; Hauser AD; Wilson JM; Williams CL; Dwinell MB

INSTITUCIÓN / INSTITUTION: - Department of Microbiology and Molecular Genetics, The Medical College of Wisconsin Cancer Center, 8701 Watertown Plank Road, Milwaukee, Wisconsin, 53226.

RESUMEN / SUMMARY: - Aggressive dissemination and metastasis of pancreatic ductal adenocarcinoma (PDAC) results in poor prognosis and marked lethality. Rho monomeric G protein levels are increased in pancreatic cancer tissue. As the mechanisms underlying PDAC malignancy are little understood, we investigated the role for cAMP in regulating monomeric G protein regulated invasion and migration of pancreatic cancer cells. Treatment of PDAC cells with cAMP elevating agents that activate adenylyl cyclases, forskolin, protein kinase A (PKA), 6-Bnz-cAMP, or the cyclic nucleotide phosphodiesterase inhibitor cilostamide significantly decreased migration and Matrigel invasion of PDAC cell lines. Inhibition was dose-dependent and not significantly different between forskolin or cilostamide treatment. cAMP elevating drugs not only blocked basal migration, but similarly abrogated transforming-growth factor-beta-directed PDAC cell migration and invasion. The inhibitory effects of cAMP were prevented by the pharmacological blockade of PKA. Drugs that increase cellular cAMP levels decreased levels of active RhoA or RhoC, with a concomitant increase in phosphorylated RhoA. Diminished Rho signaling was correlated with the appearance of thickened cortical actin bands along the perimeter of non-motile forskolin or cilostamide-treated cells. Decreased migration did not reflect alterations in cell growth or programmed cell death. Collectively these data support the notion that increased levels of cAMP specifically hinder PDAC cell motility through F-actin remodeling. © 2013 Wiley Periodicals, Inc.

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[92]

TÍTULO / TITLE: - Clinicopathologic features and prognosis of duodenal adenocarcinoma and comparison with ampullary and pancreatic ductal adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Hum Pathol. 2013 Dec;44(12):2792-8. doi: 10.1016/j.humpath.2013.07.030. Epub 2013 Oct 15.
●● Enlace al texto completo (gratuito o de pago) 1016/j.humpath.2013.07.030
AUTORES / AUTHORS: - Zenali M; Overman MJ; Rashid A; Broaddus RB; Wang H; Katz MH; Fleming JB; Abbruzzese JL; Wang H
INSTITUCIÓN / INSTITUTION: - Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030.
RESUMEN / SUMMARY: - Because of the rarity of duodenal adenocarcinoma (DAC), the clinicopathologic features and prognostication data for DAC are limited. There are no published studies directly comparing the prognosis of DAC to that of ampullary adenocarcinoma (AA) and of pancreatic ductal adenocarcinoma (PDA) after resection. In this study, we examined the clinicopathologic features of 68 patients with DAC, 92 patients with AA, and 126 patients with PDA who underwent resection. Patient clinicopathologic and survival information were extracted from medical records. Statistical analysis was performed using Statistical Package for the Social Sciences with 2-sided significance level of .05. Patients with DAC had higher American Joint Committee on Cancer (AJCC) stage than AA patients (P = .001). Lymph node metastasis (P = .013) and AJCC stage (P = .02) correlated with overall survival in DAC patients. Patients with DAC or AA had lower frequencies of lymph node metastasis and positive margin and better survival than those with PDA (P < .05). However, no differences in nodal metastasis, margin status, or survival were observed between DAC patients and those with AA. Our study showed that lymph node metastasis and AJCC stage are important prognostic factors for overall survival in DAC patients. Patients with DAC had less frequent nodal metastasis and better prognosis than those with PDA. There was no significant difference in prognosis between DAC and AA.

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[93]
TÍTULO / TITLE: - Early expression of the fractalkine receptor CX3CR1 in pancreatic carcinogenesis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Br J Cancer. 2013 Oct 29;109(9):2424-33. doi: 10.1038/bjc.2013.565. Epub 2013 Oct 1.
●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.565
AUTORES / AUTHORS: - Celesti G; Di Caro G; Bianchi P; Grizzi F; Marchesi F; Basso G; Rahal D; Delconte G; Catalano M; Cappello P; Roncalli M; Zerbi A; Montorsi M; Novelli F; Mantovani A; Allavena P; Malesci A; Laghi L
INSTITUCIÓN / INSTITUTION: - Laboratory of Molecular Gastroenterology, Department of Gastroenterology, Humanitas Clinical and Research Center, Via Manzoni, 56, 20089 Rozzano, Milan, Italy.
RESUMEN / SUMMARY: - Background:In pancreatic ductal adenocarcinoma (PDAC), fractalkine receptor CX3CR1 contributes to perineural invasion (PNI). We investigated whether CX3CR1 expression occurs early in PDAC and correlates with tumour features other than PNI.Methods:We studied CX3CR1 and CX3CL1 expression by

immunohistochemistry in 104 human PDAC and coexisting Pancreatic Intraepithelial Neoplasia (PanIN), and in PdxCre/LSL-Kras(G12D) mouse model of PDAC. CX3CR1 expression in vitro was studied by a spheroid model, and in vivo by syngenic mouse graft of tumour cells.Results:In total, 56 (53.9%) PDAC expressed CX3CR1, 70 (67.3%) CX3CL1, and 45 (43.3%) both. CX3CR1 expression was independently associated with tumour glandular differentiation (P=0.005) and PNI (P=0.01). Pancreatic Intraepithelial Neoplasias were more frequently CX3CR1+ (80.3%, P<0.001) and CX3CL1+ (86.8%, P=0.002) than matched cancers. The survival of PDAC patients was better in those with CX3CR1+ tumour (P=0.05). Mouse PanINs were also CX3CR1(+) and -CL1(+). In vitro, cytokines significantly increased CX3CL1 but not CX3CR1 expression. Differently, CX3CR1 was upregulated in tumour spheroids, and in vivo only in well-differentiated tumours.Conclusion:Tumour differentiation, rather than inflammatory signalling, modulates CX3CR1 expression in PanINs and PDAC. CX3CR1 expression pattern suggests its early involvement in PDAC progression, outlining a potential target for interfering with the PanIN transition to invasive cancer.

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[94]

TÍTULO / TITLE: - Genes-environment interactions in obesity- and diabetes-associated pancreatic cancer: A GWAS data analysis.

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

REVISTA / JOURNAL: - Cancer Epidemiol Biomarkers Prev. 2013 Oct 17.

●● Enlace al texto completo (gratuito o de pago) 1158/1055-9965.EPI-13-0437-T

AUTORES / AUTHORS: - Tang H; Wei P; Duell EJ; Risch HA; Olson SH; Bueno-de-Mesquita HB; Gallinger S; Holly EA; Petersen GM; Bracci PM; McWilliams RR; Jenab M; Riboli E; Tjonneland A; Boutron-Ruault MC; Kaaks R; Trichopoulos D; Panico S; Sund M; Peeters PH; Khaw KT; Amos CI; Li D

INSTITUCIÓN / INSTITUTION: - GI Medical Oncology, MD Anderson Cancer Center.

RESUMEN / SUMMARY: - Background: Obesity and diabetes are potentially alterable risk factors for pancreatic cancer. Genetic factors that modify the associations of obesity and diabetes with pancreatic cancer have previously not been examined at the genome-wide level. Methods: Using GWAS genotype and risk factor data from the Pancreatic Cancer Case Control Consortium, we conducted a discovery study of 2,028 cases and 2,109 controls to examine gene-obesity and gene-diabetes interactions in relation to pancreatic cancer risk by employing the likelihood ratio test (LRT) nested in logistic regression models and Ingenuity Pathway Analysis (IPA). Results: After adjusting for multiple comparisons, a significant interaction of the chemokine signaling pathway with obesity (P=3.29x10^(-6)) and a near significant interaction of calcium signaling pathway with diabetes (P=1.57x10^(-4)) in modifying the risk of pancreatic cancer was observed. These findings were supported by results from IPA analysis of the top genes with nominal interactions. The major contributing genes to the two top pathways include GNGT2, RELA, TIAM1 and GNAS. None of the individual genes or SNPs except one SNP remained significant after adjusting for multiple testing. Notably, SNP rs10818684 of the PTGS1 gene showed an interaction with diabetes (P = 7.91x10^(-7)) at a false discovery rate of 6%. Conclusions: Genetic variations in inflammatory response and insulin resistance may affect the risk of obesity and

diabetes-related pancreatic cancer. These observations should be replicated in additional large datasets. Impact: Gene-environment interaction analysis may provide new insights into the genetic susceptibility and molecular mechanisms of obesity- and diabetes-related pancreatic cancer.

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[95]
TÍTULO / TITLE: - Phenethyl Isothiocyanate Inhibits Proliferation and Induces Apoptosis in Pancreatic Cancer Cells In Vitro and in a MIAPaca2 Xenograft Animal Model.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Nutr Cancer. 2013 Nov 6.
●● Enlace al texto completo (gratuito o de pago) 1080/01635581.2013.795979
AUTORES / AUTHORS: - Stan SD; Singh SV; Whitcomb DC; Brand RE
INSTITUCIÓN / INSTITUTION: - a Department of Nutrition Science , Purdue University , West Lafayette , Indiana , USA.
RESUMEN / SUMMARY: - Pancreatic cancer is often diagnosed at an advanced stage and it has a poor prognosis that points to an increased need to develop effective chemoprevention strategies for this disease. We examined the ability of phenethyl isothiocyanate (PEITC), a naturally occurring isothiocyanate found in cruciferous vegetables, to inhibit the growth of pancreatic cancer cells in vitro and in a MIAPaca2 xenograft animal model. Exposure to PEITC inhibited pancreatic cancer cell growth in a dose-dependent manner, with an IC50 of approximately 7 mumol/L. PEITC treatment induced G2/M phase cell cycle arrest, downregulated the antiapoptotic proteins Bcl-2 and Bcl-XL, upregulated the proapoptotic protein Bak, and suppressed Notch 1 and 2 levels. In addition, treatment with PEITC induced cleavage of poly-(ADP-ribose) polymerase and led to increased cytoplasmic histone-associated DNA fragmentation and subdiploid (apoptotic) fraction in pancreatic cancer cells. Oral administration of PEITC suppressed the growth of pancreatic cancer cells in a MIAPaca2 xenograft animal model. Our data show that PEITC exerts its inhibitory effect on pancreatic cancer cells through several mechanisms, including G2/M phase cell cycle arrest and induction of apoptosis, and supports further investigation of PEITC as a chemopreventive agent for pancreatic cancer.

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[96]
TÍTULO / TITLE: - Bortezomib-induced apoptosis in cultured pancreatic cancer cells is associated with ceramide production.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Nov 5.
●● Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2318-3
AUTORES / AUTHORS: - Gong L; Yang B; Xu M; Cheng B; Tang X; Zheng P; Jing Y; Wu GJ
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Wuxi No. 2 People's Hospital, Wuxi, Jiangsu, China.
RESUMEN / SUMMARY: - PURPOSE: The proteasome inhibitor bortezomib (PS-341) has displayed significant efficiency against pancreatic cancer cells. However, the underlying mechanisms are not fully understood. Here, we tested if ceramide

production was involved in the bortezomib's effect. METHODS: Two transformed pancreatic cancer cell lines (PANC-1 and Mia) and the primary pancreatic cancer cells were used. Cell death was analyzed by MTT viability assay and trypan blue staining. Cell apoptosis was analyzed by Histone DNA-ELISA assay and Annexin V FACS. Western blots were used to test signal protein changes. The cellular ceramide level after bortezomib treatment was also determined. RESULTS: In cultured pancreatic cancer cells, bortezomib increased cellular ceramide production to promote cell apoptosis. The ceramide de novo synthase inhibitor fumonisin B1 (F-B1) suppressed bortezomib-induced ceramide production and apoptosis, while exogenously added C6-ceramide facilitated bortezomib-induced pancreatic cancer cell death. Meanwhile, 1-phenyl-2-decanoylamino-3-morpholino-1-propanol (PDMP), the inhibitor of glucosylceramide synthetase as well as the sphingosine kinase 1 inhibitors (SKI-II and SKI-IV), facilitated bortezomib-induced ceramide production and subsequent cell apoptosis. Further, bortezomib-induced pro-apoptotic c-Jun N-terminal kinase (JNK) activation was also associated with ceramide production. JNK activation by bortezomib was suppressed by F-B1, but was enhanced by SKI-II and PDMP in pancreatic cancer cells. Finally, C6-ceramide, SKI-II, and PDMP dramatically enhanced bortezomib-induced cytotoxicity in primary cultured pancreatic cancer cells. CONCLUSIONS: We found that bortezomib-induced apoptosis was associated with ceramide production in primary and transformed pancreatic cancer cells.

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[97]

TÍTULO / TITLE: - Novel synthetic oleanane triterpenoid AMR-MeOAc inhibits K-Ras through ERK, Akt and survivin in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Phytomedicine. 2013 Nov 8. pii: S0944-7113(13)00404-2. doi: 10.1016/j.phymed.2013.09.017.

●● Enlace al texto completo (gratuito o de pago) 1016/j.phymed.2013.09.017

AUTORES / AUTHORS: - Rabi T; Venkatanarashiman M

INSTITUCIÓN / INSTITUTION: - Siddha Clinic and Research Center SVA, Kanyakumari, India. Electronic address: thangaiyanrabi@hotmail.com.

RESUMEN / SUMMARY: - K-Ras activating mutations are a major problem that drives aggressive tumor growth and metastasis in pancreatic cancer. Currently, there are no effective targeted therapies for this genetically defined subset of cancers harboring oncogenic K-Ras mutations that confer drug resistance, aggressive tumor growth, metastasis and poor clinical outcome. We identified a novel synthetic oleanane triterpenoid compound designated AMR-MeOAc that effectively kills K-Ras mutant pancreatic cancer HPAF-II cells. The cytotoxic effects correlated with apoptosis induction, as was evidenced by increase of apoptosis cells upon the treatment of AMR-MeOAc in HPAF-II cells. Our studies revealed that AMR-MeOAc treatment inhibits cancer associated survival gene survivin. Moreover, AMR-MeOAc also led to down regulation of Akt, ERK1/2 and survivin protein levels. Our results indicate that AMR-MeOAc or its active analogs could be a novel class of anticancer agents against K-Ras driven human pancreatic cancer.

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[98]

TÍTULO / TITLE: - Reverse-Phase Protein Array Analysis to Identify Biomarker Proteins in Human Pancreatic Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Dig Dis Sci. 2013 Nov 19.
●● Enlace al texto completo (gratuito o de pago) 1007/s10620-013-2938-9
AUTORES / AUTHORS: - Huang YJ; Frazier ML; Zhang N; Liu Q; Wei C
INSTITUCIÓN / INSTITUTION: - Department of Epidemiology, Unit 1365, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX, 77030, USA, yjhuang@mdanderson.org.
RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is the fourth leading cause of cancer death in the United States. The high mortality rate of patients with pancreatic cancer is primarily due to the difficulty of early diagnosis and a lack of effective therapies. There is an urgent need to discover novel molecular targets for early diagnosis and new therapeutic approaches to improve the clinical outcome of this deadly disease. AIM: We utilized the reverse-phase protein assay (RPPA) to identify differentially expressed biomarker proteins in tumors and matched adjacent, normal-appearing tissue samples from 15 pancreatic cancer patients. METHODS: The antibody panel used for the RPPA included 130 key proteins involved in various cancer-related pathways. The paired t test was used to determine the significant differences between matched pairs, and the false discovery rate-adjusted p values were calculated to take into account the effect of multiple comparisons. RESULTS: After correcting for multiple comparisons, we found 19 proteins that had statistically significant differences in expression between matched pairs. However, only four (AKT, beta-catenin, GAB2, and PAI-1) of them met the conservative criteria (both a q value <0.05 and a fold-change of >/=3/2 or </=2/3) to be considered differentially expressed. Overexpression of AKT, beta-catenin, and GAB2 in pancreatic cancer tissues identified by RPPA has also been further confirmed by western blot analysis. Further analysis identified several significantly associated canonical pathways and overrepresented network functions. CONCLUSION: GAB2, a newly identified protein in pancreatic cancer, may provide additional insight into this cancer's pathogenesis. Future studies in a larger population are warranted to further confirm our results.

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[99]
TÍTULO / TITLE: - Bufalin exerts antitumor effects by inducing cell cycle arrest and triggering apoptosis in pancreatic cancer cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 12.
●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-1326-6
AUTORES / AUTHORS: - Li M; Yu X; Guo H; Sun L; Wang A; Liu Q; Wang X; Li J
INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Cancer Center, Qilu Hospital, Shandong University, Jinan, 250012, China.
RESUMEN / SUMMARY: - As one of the most aggressive human malignancies, pancreatic cancer is a leading cause of cancer-related deaths worldwide and only about 4 % of patients will live 5 years after diagnosis. Eighty to approximately eighty-five percent of patients are diagnosed with an unresectable or metastatic disease, which is correlated with poor prognosis and low survival rate. Therefore, it is tremendously significant to exploit novel chemicals to prevent and treat pancreatic

cancer. Previous research and clinical studies have demonstrated that many natural products derived from traditional Chinese medicine (TCM) such as camptothecin derivatives and vinca alkaloids could be effective antitumor compounds, hinting that TCM is a promising source for developing new antitumor drugs. In this report, we investigated the effects of bufalin, a primary active ingredient of the traditional Chinese medicine Chan-Su, on pancreatic cancer cell lines PANC-1 and CFPAC-1 and studied the underlying molecular mechanism. We found that exposure to bufalin could suppress the proliferation of pancreatic cancer cells time and dose dependently. We used flow cytometry to study the effects of bufalin on apoptosis and cell cycle distribution in PANC-1 and CFPAC-1 cells. The results indicated that bufalin could significantly induce both apoptosis and G2/M cell cycle arrest in pancreatic cancer cells. With western blotting, we found that the expression level of an antiapoptotic protein heat shock protein 27 (Hsp27) and its partner molecule p-Akt was decreased upon the treatment with bufalin. Besides, bufalin activated pro-caspase-3 and pro-caspase-9 and modulated the expression level of Bcl-2 and Bax. These data suggested that bufalin may trigger apoptosis by targeting Hsp27, which could inhibit apoptosis by interfering with key apoptotic proteins. The influence on the level of cylinB1, CDK1, and p21 was also observed after bufalin treatment, and the relationship between Hsp27 and the cell cycle-related proteins mentioned above deserves much more research. In addition, our data showed that bufalin could enhance the growth inhibition effect of gemcitabine in above pancreatic cancer cells. Taken together, bufalin might be worthy of further study for its potential as a therapeutic agent for pancreatic cancer treatment.

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[100]

TÍTULO / TITLE: - Positron emission tomography study on pancreatic somatostatin receptors in normal and diabetic rats with Ga-DOTA-octreotide: A potential PET tracer for beta cell mass measurement.

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

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Nov 9. pii: S0006-291X(13)01874-3. doi: 10.1016/j.bbrc.2013.11.001.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bbrc.2013.11.001

AUTORES / AUTHORS: - Sako T; Hasegawa K; Nishimura M; Kanayama Y; Wada Y; Hayashinaka E; Cui Y; Kataoka Y; Senda M; Watanabe Y

INSTITUCIÓN / INSTITUTION: - Division of Bio-function Dynamics Imaging, RIKEN Center for Life Science Technologies, 6-7-3 Minatojima-minamimachi, Chuo-ku, Kobe, Hyogo 650-0047, Japan; Division of Molecular Imaging, Institute of Biomedical Research and Innovation, 2-2 Minatojima-minamimachi, Chuo-ku, Kobe, Hyogo 650-0047, Japan; Kobe University Graduate School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe, Hyogo 650-0017, Japan.

RESUMEN / SUMMARY: - Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia, and the loss or dysfunction of pancreatic beta cells has been reported before the appearance of clinical symptoms and hyperglycemia. To evaluate beta cell mass (BCM) for improving the detection and treatment of DM at earlier stages, we focused on somatostatin receptors that are highly expressed in the pancreatic beta cells, and developed a positron emission tomography (PET) probe derived from octreotide, a metabolically stable somatostatin analog. Octreotide was

conjugated with 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA), a chelating agent, and labeled with 68Gallium (68Ga). After intravenous injection of 68Ga-DOTA-octreotide, a 90-min emission scan of the abdomen was performed in normal and DM model rats. The PET studies showed that 68Ga-DOTA-octreotide radioactivity was highly accumulated in the pancreas of normal rats and that the pancreatic accumulation was significantly reduced in the rats administered with an excess amount of unlabeled octreotide or after treatment with streptozotocin, which was used for the chemical induction of DM in rats. These results were in good agreement with the ex vivo biodistribution data. These results indicated that the pancreatic accumulation of 68Ga-DOTA-octreotide represented specific binding to the somatostatin receptors and reflected BCM. Therefore, PET imaging with 68Ga-DOTA-octreotide could be a potential tool for evaluating BCM.

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[101]

TÍTULO / TITLE: - Penetrance of functioning and non-functioning pancreatic neuroendocrine tumors in multiple endocrine neoplasia type 1 in the second decade of life.

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

REVISTA / JOURNAL: - J Clin Endocrinol Metab. 2013 Oct 31.

●● Enlace al texto completo (gratuito o de pago) 1210/jc.2013-1768

AUTORES / AUTHORS: - Goncalves TD; Toledo RA; Sekiya T; Matuguma SE; Maluf Filho F; Rocha MS; Siqueira SA; Glezer A; Bronstein MD; Pereira Ricardo Jureidini MA; Bacchella T; Machado MC; Toledo SP; Lourenco DM Jr

INSTITUCIÓN / INSTITUTION: - Endocrine Genetics Unit (LIM-25) (T.D.G., R.A.T.*, T.S., S.P.A.T., D.M.L.J.), Endocrinology Division (T.D.G., R.A.T., T.S., A.G., M.D.B., M.A.A.P., S.P.A.T., D.M.L.J.), Endoscopy Division (S.E.M., F.M.F.), Radiology Division (M.S.R.), Pathology Division (S.A.C.S.), Department of Gastroenterology, Surgical Division (T.B., M.C.C.M.), Hospital das Clinicas, University of Sao Paulo School of Medicine; Department of Gastroenterology, Surgical Division (T.B., R.J.) and Endocrine Oncology Division, Cancer Institute of Sao Paulo (D.M.L.J.), Sao Paulo, Brazil.; * R.A.T is now at Division of Hematology and Medical Oncology, Department of Medicine, Cancer Therapy and Research Center at the University of Texas Health Science Center, 7703 Floyd Curl Dr, MC 7880, San Antonio, TX 78229-3900, USA.

RESUMEN / SUMMARY: - Context:Data are scarce on penetrance of multiple endocrine neoplasia type 1 (MEN1)-related non-functioning pancreatic neuroendocrine tumors (NF-PETs) and insulinomas in young MEN1 patients. A potential positive correlation between tumor size and malignancy (2-3cm, 18%; >3cm, 43%) has greatly influenced the management of MEN1 adults with NF-PETs.Objective:To estimate the penetrance of NF-PETs, insulinomas and gastrinomas in young MEN1 carriers.Design:The data were obtained from a screening program (1996-2012) involving 113 MEN1 patients (tertiary academic reference center).Patients:Nineteen MEN1 patients (aged 12-20y; 16 patients aged 15-20y and 3 patients aged 12-14y) were screened for NF-PETs, insulinomas and gastrinomas.Methods:MRI/CT and endoscopic US (EUS) were performed on 10 MEN1 carriers, MRI/CT was performed on five patients, and four other patients underwent an EUS.Results:The overall penetrance of PETs during the second decade of life was 42% (8/19). All eight PET patients had NF-PETs, and half of those tumors were multicentric. One-fifth of the screened patients (21%; 4/19)

harbored at least one large tumor (>2.0cm). Insulinoma was detected in two NF-PET patients (11%) at the initial screening; gastrinoma was not present in any cases. Six of the 11 (54%) screened patients aged 15-20y who underwent an EUS had NF-PETs. Potential false-positive EUS results were excluded based on EUS-guided biopsy results, the reproducibility of the NF-PET findings or the observation of increased tumor size during follow-up. Distal pancreatectomy and the nodule enucleation of pancreatic head tumors were conducted on three patients with large tumors (>2.0cm; T2N0M0) that were classified as grade 1 neuroendocrine tumors (Ki-67<2%).Conclusions:Our data demonstrated high penetrance of NF-PETs in 15-20-y-old MEN1 patients. The high percentage of the patients presenting consensus criteria for surgery for NF-PET alone or NF-PET/insulinoma suggests a potential benefit for the periodic surveillance of these tumors in this age group.

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[102]

TÍTULO / TITLE: - Ellagic Acid and embelin affect key cellular components of pancreatic adenocarcinoma, cancer, and stellate cells.

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

REVISTA / JOURNAL: - Nutr Cancer. 2013;65(8):1232-44. doi: 10.1080/01635581.2013.832779. Epub 2013 Oct 15.

●● Enlace al texto completo (gratuito o de pago) 1080/01635581.2013.832779

AUTORES / AUTHORS: - Edderkaoui M; Lugea A; Hui H; Eibl G; Lu QY; Moro A; Lu X; Li G; Go VL; Pandol SJ

INSTITUCIÓN / INSTITUTION: - a Veterans Affairs Greater Los Angeles Healthcare System , Los Angeles , California , USA.

RESUMEN / SUMMARY: - Ellagic acid is a polyphenolic phytochemical present in many fruits and nuts with anticancer properties demonstrated in experimental tumor studies. Embelin is a benzoquinone phytochemical isolated from the Japanese herb Ardisiae Japonicae and has been shown to induce apoptosis in cancer cells. We found that ellagic acid and embelin each dose-dependently increased apoptosis and inhibited proliferation in human pancreatic cancer cells, MIA PaCa-2 and HPAF-II cells, and in pancreatic stellate cells, which are progenitors of pancreatic cancer desmoplasia. In each of these cell types, combinations of ellagic acid and embelin at low micromolar concentrations (0.5-3 muM) induced synergistic increases in apoptosis and decreases in proliferation. Ellagic acid decreased NF-kappaB transcriptional activity, whereas embelin decreased STAT-3 phosphorylation and protein expression of its downstream target survivin in cancer cells. In vivo dietary ellagic acid alone or in combination with embelin decreased tumor size and tumor cellularity in a subcutaneous xenograft mouse model of pancreatic cancer. These results show that ellagic acid and embelin interact with divergent intracellular signaling pathways resulting in augmentation of apoptosis and inhibition of proliferation at low micromolar concentrations for the key cellular components of pancreatic adenocarcinoma.

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[103]

TÍTULO / TITLE: - Catheter-based and endoluminal ultrasound applicators for magnetic resonance image-guided thermal therapy of pancreatic cancer: Preliminary investigations.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Acoust Soc Am. 2013 Nov;134(5):4089. doi: 10.1121/1.4830933.

●● Enlace al texto completo (gratuito o de pago) 1121/1.4830933

AUTORES / AUTHORS: - Diederich C; Salgaonkar V; Prakash P; Adams M; Scott S; Jones P; Hensley D; Chen H; Plata J; Holbrook A; Butts Pauly K; Sommer G
INSTITUCIÓN / INSTITUTION: - Radiation Oncology, UCSF, 1600 Divisadero St., Ste. H1031, San Francisco, CA 94143-1708 cdiederich@radonc.ucsf.edu.
RESUMEN / SUMMARY: - Ultrasound devices are being investigated for endoluminal and intraductal access for targeted thermal ablation or hyperthermia of pancreas under MR guidance and temperature monitoring. Simulations using patient-specific 3D models were developed for applicator design and development of treatment delivery strategies. MR-compatible devices were constructed for endoluminal (3-5 MHz planar or lightly focused rectangular elements, 12-mm OD assembly, expandable balloon), transgastric interstitial and intraductal (6-8 MHz multi-sectored tubular elements, 2-mm catheter) deployment. Micro-coils were integrated for active MR tracking of position and alignment. The proof-of-concept devices were tested in phantoms, ex vivo tissues, cadaveric porcine models, and in vivo animal models under 3T MR temperature imaging (MRTI). Results indicate endoluminal devices could ablate 2-2.5 cm depth from gastric wall for tumors of the pancreatic head, and multi-sectored tubular intraductal and interstitial applicators could ablate 2.3-3.4 cm diameter targets with directional control. Intraductal applicators could produce effective hyperthermia (>40 C) extending 15 mm radial. Customized tracking sequences could be used to locate 3D position of the applicators. Endoluminal, interstitial, and intraductal ultrasound applicators show promise for ablation or hyperthermia of pancreatic tumors. MR guidance can be employed for positioning these devices with active tracking coils and real time temperature monitoring. (NIH-P01CA159992.).

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[104]
TÍTULO / TITLE: - Treatment of hemorraghic pancreatic pseudocyst by selective embolization of the splenic artery.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cir Esp. 2013 Oct 9. pii: S0009-739X(13)00277-7. doi: 10.1016/j.ciresp.2013.04.022.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ciresp.2013.04.022

AUTORES / AUTHORS: - Arencibia Perez B; Hidalgo Rodriguez MA; Gonzalez de Chavez Rodriguez PE; Chocarro Huesa C
INSTITUCIÓN / INSTITUTION: - Servicio de Cirugia General y Aparato Digestivo, Hospital Universitario Nuestra Senora de Candelaria, Santa Cruz de Tenerife, España. Electronic address: bearenci@gmail.com.

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[105]
TÍTULO / TITLE: - Capsaicin induces cytotoxicity in pancreatic neuroendocrine tumor cells via mitochondrial action.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Cell Signal. 2014 Jan;26(1):41-8. doi: 10.1016/j.cellsig.2013.09.014. Epub 2013 Sep 27.

●● Enlace al texto completo (gratuito o de pago) 1016/j.cellsig.2013.09.014

AUTORES / AUTHORS: - Skrzypski M; Sassek M; Abdelmessih S; Mergler S; Grotzinger C; Metzke D; Wojciechowicz T; Nowak KW; Strowski MZ

INSTITUCIÓN / INSTITUTION: - Department of Hepatology and Gastroenterology & the Interdisciplinary Centre of Metabolism: Endocrinology, Diabetes and Metabolism, Charite-University Medicine Berlin, 13353 Berlin, Germany; Department of Animal Physiology and Biochemistry, Poznan University of Life Sciences, 60-637 Poznan, Poland. Electronic address: marek.skrzypski@charite.de.

RESUMEN / SUMMARY: - Capsaicin (CAP), the pungent ingredient of chili peppers, inhibits growth of various solid cancers via TRPV1 as well as TRPV1-independent mechanisms. Recently, we showed that TRPV1 regulates intracellular calcium level and chromogranin A secretion in pancreatic neuroendocrine tumor (NET) cells. In the present study, we characterize the role of the TRPV1 agonist - CAP - in controlling proliferation and apoptosis of pancreatic BON and QGP-1 NET cells. We demonstrate that CAP reduces viability and proliferation, and stimulates apoptotic death of NET cells. CAP causes mitochondrial membrane potential loss, inhibits ATP synthesis and reduces mitochondrial Bcl-2 protein production. In addition, CAP increases cytochrome c and cleaved caspase 3 levels in cytoplasm. CAP reduces reactive oxygen species (ROS) generation. The antioxidant N-acetyl-l-cysteine (NAC) acts synergistically with CAP to reduce ROS generation, without affecting CAP-induced toxicity. TRPV1 protein reduction by 75% reduction fails to attenuate CAP-induced cytotoxicity. In summary, these results suggest that CAP induces cytotoxicity by disturbing mitochondrial potential, and inhibits ATP synthesis in NET cells. Stimulation of ROS generation by CAP appears to be a secondary effect, not related to CAP-induced cytotoxicity. These results justify further evaluation of CAP in modulating pancreatic NETs in vivo.

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[106]

TÍTULO / TITLE: - Effect of hyperbaric oxygenation and gemcitabine on apoptosis of pancreatic ductal tumor cells in vitro.

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

REVISTA / JOURNAL: - Anticancer Res. 2013 Nov;33(11):4827-32.

AUTORES / AUTHORS: - Bosco G; Guizzon L; Yang Z; Camporesi E; Casarotto A; Bosio C; Mangar D; Chen C; Cannato M; Toniolo L; Garetto G; Nasole E; Bassi C

INSTITUCIÓN / INSTITUTION: - Department of Anesthesiology, SUNY Upstate Medical University, Syracuse, NY, 13210, U.S.A. yangz@upstate.edu.

RESUMEN / SUMMARY: - BACKGROUND: Gemcitabine is first-line therapy for advanced pancreatic ductal adenocarcinoma (PDAC) with a poor survival and response rate. Hyperbaric oxygenation (HBO) enhances delivery of oxygen to hypoxic tumor cells and increases their susceptibility to cytotoxic effects of chemotherapy. We hypothesized that the anticancer activity of gemcitabine (GEM) may be enhanced if tumor cells are placed in an oxygen-rich environment. The present study evaluated the effects of gemcitabine, HBO and their combination on apoptosis of tumor cells. MATERIALS AND METHODS: PANC-1 and AsPc-1 PDAC tumor cell lines were used. Cultured tumor cells were treated with GEM at its growth-inhibitory concentration (IC50) and HBO at 2.5 ATA for 90 min or a combination of both (HBO then GEM and

GEM then HBO). Twenty-four hours later, apoptotic cells in each group were analyzed and the apoptotic index (AI) was calculated. RESULTS: PANC-1 cell line: HBO alone had no effect on AI: 6.5+/-0.1 vs. 5.9+/-0.1. HBO before and after gemcitabine did not further increase AI: 8.2+/-0.1 (HBO-GEM), 8.5+/-0.1 (GEM-HBO) vs. 8.1+/-0.1 (GEM). The combination of HBO and gemcitabine significantly increased AI: 10.7+/-0.02 ($p<0.001$ vs. all groups). AsPc-1 cell line: HBO-alone had no effect on AI: 5.9+/-0.1 vs. 5.9+/-0.1. HBO before and after gemcitabine did not further increase AI: 8.2+/-0.1 (HBO-GEM), 8.4+/-0.1 (GEM-HBO) vs. 8.0+/-0.1 (GEM). The combination of HBO and gemcitabine significantly increased AI: 9.7+/-0.1 ($p<0.001$ vs. all groups). CONCLUSION: HBO-alone, whether administered before and after gemcitabine has no effect on apoptosis of PDAC cells in vitro. HBO significantly enhanced gemcitabine-induced apoptosis when administered during gemcitabine. Our findings suggest that the time window would be critical for using HBO as adjuvant to chemotherapy.

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[107]

TÍTULO / TITLE: - Targeting elongation factor-2 kinase (eEF-2K) induces apoptosis in human pancreatic cancer cells.

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

REVISTA / JOURNAL: - Apoptosis. 2013 Nov 6.

●● Enlace al texto completo (gratuito o de pago) 1007/s10495-013-0927-2

AUTORES / AUTHORS: - Ashour AA; Abdel-Aziz AA; Mansour AM; Alpay SN; Huo L; Ozpolat B

INSTITUCIÓN / INSTITUTION: - Department of Experimental Therapeutics, Unit 422, The University of Texas, M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX, 77030, USA.

RESUMEN / SUMMARY: - Pancreatic cancer (PaCa) is one of the most aggressive, apoptosis-resistant and currently incurable cancers with a poor survival rate. Eukaryotic elongation factor-2 kinase (eEF-2K) is an atypical kinase, whose role in PaCa survival is not yet known. Here, we show that eEF-2K is overexpressed in PaCa cells and its down-regulation induces apoptotic cell death. Rottlerin (ROT), a polyphenolic compound initially identified as a PKC-delta inhibitor, induces apoptosis and autophagy in a variety of cancer cells including PaCa cells. We demonstrated that ROT induces intrinsic apoptosis, with dissipation of mitochondrial membrane potential (DeltaPsim), and stimulates extrinsic apoptosis with concomitant induction of TNF-related apoptosis inducing ligand (TRAIL) receptors, DR4 and DR5, with caspase-8 activation, in PANC-1 and MIAPaCa-2 cells. Notably, while none of these effects were dependent on PKC-delta inhibition, ROT down-regulates eEF-2K at mRNA level, and induce eEF-2K protein degradation through ubiquitin-proteasome pathway. Down-regulation of eEF-2K recapitulates the events observed after ROT treatment, while its over-expression suppressed the ROT-induced apoptosis. Furthermore, eEF-2K regulates the expression of tissue transglutaminase (TG2), an enzyme previously implicated in proliferation, drug resistance and survival of cancer cells. Inhibition of eEF-2K/TG2 axis leads to caspase-independent apoptosis which is associated with induction of apoptosis-inducing factor (AIF). Collectively, these results indicate, for the first time, that the down-regulation of eEF-2K leads to induction of intrinsic, extrinsic as well as AIF-dependent apoptosis in PaCa cells, suggesting that eEF-2K may represent an attractive therapeutic target for the future anticancer agents in PaCa.

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[108]

TÍTULO / TITLE: - Grading of well-differentiated pancreatic neuroendocrine tumors is improved by the inclusion of both Ki67 proliferative index and mitotic rate.

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

REVISTA / JOURNAL: - Am J Surg Pathol. 2013 Nov;37(11):1671-7. doi: 10.1097/PAS.0000000000000089.

●● Enlace al texto completo (gratuito o de pago)

1097/PAS.0000000000000089

AUTORES / AUTHORS: - McCall CM; Shi C; Cornish TC; Klimstra DS; Tang LH; Basturk O; Mun LJ; Ellison TA; Wolfgang CL; Choti MA; Schulick RD; Edil BH; Hruban RH

INSTITUCIÓN / INSTITUTION: - Departments of *Pathology section signSurgery, The Sol Goldman Pancreatic Cancer Research Center, The Johns Hopkins University School of Medicine, Baltimore, MD daggerDepartment of Pathology, Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN double daggerDepartment of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY parallelDepartment of Surgery, University of Colorado Anschutz Medical Campus, Aurora, CO.

RESUMEN / SUMMARY: - The grading system for pancreatic neuroendocrine tumors (PanNETs) adopted in 2010 by the World Health Organization (WHO) mandates the use of both mitotic rate and Ki67/MIB-1 index in defining the proliferative rate and assigning the grade. In cases when these measures are not concordant for grade, it is recommended to assign the higher grade, but specific data justifying this approach do not exist. Thus, we counted mitotic figures and immunolabeled, using the Ki67 antibody, 297 WHO mitotic grade 1 and 2 PanNETs surgically resected at a single institution. We quantified the Ki67 proliferative index by marking at least 500 cells in “hot spots” and by using digital image analysis software to count each marked positive/negative cell and then compared the results with histologic features and overall survival. Of 264 WHO mitotic grade 1 PanNETs, 33% were WHO grade 2 by Ki67 proliferative index. Compared with concordant grade 1 tumors, grade-discordant tumors were more likely to have metastases to lymph node (56% vs. 34%) ($P<0.01$) and to distant sites (46% vs. 12%) ($P<0.01$). Discordant mitotic grade 1 PanNETs also showed statistically significantly more infiltrative growth patterns, perineural invasion, and small vessel invasion. Overall survival was significantly different ($P<0.01$), with discordant mitotic grade 1 tumors showing a median survival of 12 years compared with 16.7 years for concordant grade 1 tumors. Conversely, mitotic grade 1/Ki67 grade 2 PanNETs showed few significant differences from tumors that were mitotic grade 2 and either Ki67 grade 1 or 2. Our data demonstrate that mitotic rate and Ki67-based grades of PanNETs are often discordant, and when the Ki67 grade is greater than the mitotic grade, clinical outcomes and histopathologic features are significantly worse than concordant grade 1 tumors. Patients with discordant mitotic grade 1/Ki67 grade 2 tumors have shorter overall survival and larger tumors with more metastases and more aggressive histologic features. These data strongly suggest that Ki67 labeling be performed on all PanNETs in addition to mitotic rate determination to define more accurately tumor grade and prognosis.

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[109]

TÍTULO / TITLE: - Suppressed expression of NDRG2 correlates with poor prognosis in pancreatic cancer.

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

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Nov 8;441(1):102-7. doi: 10.1016/j.bbrc.2013.10.010. Epub 2013 Oct 14.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bbrc.2013.10.010

AUTORES / AUTHORS: - Yamamura A; Miura K; Karasawa H; Morishita K; Abe K; Mizuguchi Y; Saiki Y; Fukushige S; Kaneko N; Sase T; Nagase H; Sunamura M; Motoi F; Egawa S; Shibata C; Unno M; Sasaki I; Horii A

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Tohoku University, Graduate School of Medicine, Sendai, Japan; Department of Pathology, Tohoku University, Graduate School of Medicine, Sendai, Japan.

RESUMEN / SUMMARY: - Pancreatic cancer is a highly lethal disease with a poor prognosis; the molecular mechanisms of the development of this disease have not yet been fully elucidated. N-myc downstream regulated gene 2 (NDRG2), one of the candidate tumor suppressor genes, is frequently downregulated in pancreatic cancer, but there has been little information regarding its expression in surgically resected pancreatic cancer specimens. We investigated an association between NDRG2 expression and prognosis in 69 primary resected pancreatic cancer specimens by immunohistochemistry and observed a significant association between poor prognosis and NDRG2-negative staining (P=0.038). Treatment with trichostatin A, a histone deacetylase inhibitor, predominantly up-regulated NDRG2 expression in the NDRG2 low-expressing cell lines (PANC-1, PCI-35, PK-45P, and AsPC-1). In contrast, no increased NDRG2 expression was observed after treatment with 5-aza-2' deoxycytidine, a DNA demethylating agent, and no hypermethylation was detected in either pancreatic cancer cell lines or surgically resected specimens by methylation specific PCR. Our present results suggest that (1) NDRG2 is functioning as one of the candidate tumor-suppressor genes in pancreatic carcinogenesis, (2) epigenetic mechanisms such as histone modifications play an essential role in NDRG2 silencing, and (3) the expression of NDRG2 is an independent prognostic factor in pancreatic cancer.

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[110]

TÍTULO / TITLE: - Neoadjuvant Chemoradiation and Duration of Chemotherapy Before Surgical Resection for Pancreatic Cancer: Does Time Interval Between Radiotherapy and Surgery Matter?

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Nov 26.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3396-5

AUTORES / AUTHORS: - Chen KT; Devarajan K; Milestone BN; Cooper HS; Denlinger C; Cohen SJ; Meyer JE; Hoffman JP

INSTITUCIÓN / INSTITUTION: - Department of Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA, USA, kathryn.chen@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: Neoadjuvant chemoradiation and chemotherapy provided for borderline or locally advanced, potentially resectable

pancreatic adenocarcinoma improves resectability rates. Response to therapy is also an important prognostic factor. There are no data in the literature regarding optimal time interval or duration of chemotherapy after chemoradiation before surgery, and pathologic response rates. Using our database, we evaluated these relationships and the effect on overall and progression-free survival. METHODS: We retrospectively analyzed the records of 83 patients who underwent neoadjuvant chemoradiation for locally advanced, potentially resectable, and borderline resectable pancreatic cancers before definitive resection. We divided patients into three groups according to time interval between completion of chemoradiation and resection: group A (0-10 weeks), group B (11-20 weeks), and group C (>20 weeks). After chemoradiation, patients underwent ongoing chemotherapy before resection. Pathologic response was defined as major (>95 % fibrosis), partial (50-94 % fibrosis), or minor (<50 % fibrosis). RESULTS: There were 56 patients in group A, 17 patients in group B, and 10 patients in group C. Patients in groups B and C were significantly more likely to experience a major response than group A ($p < 0.013$). Patients in group C had significantly increased median progression-free and overall survival ($p < 0.05$). Multivariable classification and regression tree analysis demonstrated pathologic response to be the only significant factor in overall survival. CONCLUSIONS: Patients who underwent a prolonged time interval after neoadjuvant chemoradiation with ongoing chemotherapy were more likely to have an improved pathologic response at time of surgical resection, which was associated with improved median overall survival.

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[111]

TÍTULO / TITLE: - EGFR expression in pancreatic adenocarcinoma. Relationship to tumour morphology and cell adhesion proteins.

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

REVISTA / JOURNAL: - J Clin Pathol. 2013 Oct 29. doi: 10.1136/jclinpath-2013-201662.

●● Enlace al texto completo (gratuito o de pago) 1136/jclinpath-2013-201662

AUTORES / AUTHORS: - Handra-Luca A; Hammel P; Sauvanet A; Lesty C; Ruszniewski P; Couvelard A

INSTITUCIÓN / INSTITUTION: - Departement d'Anatomie pathologique, APHP Hopital Avicenne, Bobigny, France.

RESUMEN / SUMMARY: - AIMS: We aimed to study epidermal growth factor receptor (EGFR) expression in surgically resected pancreatic ductal adenocarcinomas (PDACs) by immunohistochemistry and their relationship to clinicopathological features, cell proliferation and cell adhesion protein expression. METHODS: A total of 99 PDACs were analysed on tissue microarrays for EGFR, E-cadherin and beta-catenin expression patterns in tumour cells. The percentage of cells expressing the three proteins (membrane, cytoplasm or nuclear pattern) and of Ki67-positive tumour cells was assessed. Tumour protein expression was studied with regard to clinicomorphological features, Ki67 index and for postsurgical survival. RESULTS: Membrane tumour EGFR correlated with histological poor differentiation (dedifferentiation), increased number of mitoses and severe tumour cell atypia (pleiomorphism) as well as with aberrant adhesion protein expression such as nuclear beta-catenin and cytoplasmic E-cadherin. Cytoplasmic tumour E-cadherin correlated with an increased Ki67-positive tumour cell component, whereas nuclear E-cadherin

correlated with a shorter postsurgical overall survival, as well as with tumour necrosis and an abundant clear cell component. CONCLUSIONS: In conclusion, the results of our study suggest a complex role for EGFR in PDAC carcinogenesis, tumour expression of this protein being associated with tumour dedifferentiation, mitotic activity or pleiomorphism, as well as with aberrant tumour cell adhesion protein expression.

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[112]

TÍTULO / TITLE: - NOV promoted the growth and migration of pancreatic cancer cells.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 21.

●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-1418-3

AUTORES / AUTHORS: - Cui L; Xie R; Dang S; Zhang Q; Mao S; Chen J; Qu J; Zhang J

INSTITUCIÓN / INSTITUTION: - General Surgery Department, Affiliated hospital, Jiangsu University, Zhenjiang, Jiangsu, China.

RESUMEN / SUMMARY: - NOV, a member of the CCN (Cyr61, CTGF and NOV) family, is involved in diverse biological processes, such as cell adhesion, proliferation and angiogenesis. However, its function in pancreatic cancer remains poorly understood. Here, we found that the expression of NOV was up-regulated in pancreatic cancer tissues. Moreover, over-expression of NOV in pancreatic cancer cells promoted cell proliferation and migration, while knock down the expression of NOV impaired the tumorigenecity of pancreatic cancer cells in vitro and in vivo. Mechanistically, NOV induced epithelial-mesenchymal transition (EMT) and regulated the expression of multiple EMT marker. Taken together, our study suggested the important role of NOV in pancreatic cancer and NOV might be an important therapeutic target.

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[113]

TÍTULO / TITLE: - Cyclooxygenase 2 promoted the tumorigenecity of pancreatic cancer cells.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 22.

●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-1301-2

AUTORES / AUTHORS: - Li W; Mao Z; Fan X; Cui L; Wang X

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Affiliated Hospital of Jiangsu University, Zhenjiang, Jiangsu Province, China.

RESUMEN / SUMMARY: - Pancreatic cancer is one of the leading causes of cancer-related death in the world. It is very urgent to find new therapeutic targets and improve the treatment. Cyclooxygenase 2 (Cox2), a regulator of inflammation signaling, has been found to be involved in tumorigenesis of various tumor types. However, its biological functions in pancreatic cancer cells are not fully understood. Here, we found that the expression of Cox2 was elevated in pancreatic cancer tissues compared with that in the paired normal tissues. The over-expression of Cox2 in pancreatic cancer cells promoted cell proliferation and migration, while the knockdown of the expression of Cox2 inhibited the tumorigenesis of pancreatic cancer cells in vitro and in vivo. Mechanistically, Cox2 regulated the expression of multiple genes involved in cell growth, migration, and cell apoptosis. Taken together, our study revealed the pivotal

function of Cox2 in pancreatic cancer, and Cox2 might be an important therapeutic target for the treatment.

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[114]
TÍTULO / TITLE: - Targeting metabolic scavenging in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Cancer Res. 2013 Oct 28.
●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-2570
AUTORES / AUTHORS: - Lyssiotis CA; Cantley LC
INSTITUCIÓN / INSTITUTION: - Medicine, Weill Cornell Medical College.
RESUMEN / SUMMARY: - Pancreatic tumor metabolism is rewired to facilitate survival and growth in a nutrient-depleted environment. This leads to a unique dependence on metabolic recycling and scavenging pathways, including NAD salvage. Targeting this pathway in pancreatic cancer disrupts metabolic homeostasis and impairs tumor growth.

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[115]
TÍTULO / TITLE: - Nox4-derived ROS signaling contributes to TGF-beta-induced epithelial-mesenchymal transition in pancreatic cancer cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Anticancer Res. 2013 Oct;33(10):4431-8.
AUTORES / AUTHORS: - Hiraga R; Kato M; Miyagawa S; Kamata T
INSTITUCIÓN / INSTITUTION: - Department of Molecular Biology and Biochemistry, Shinshu University Graduate School of Medicine, 3-1-1 Asahi, Matsumoto, Nagano 390-8621, Japan. kamatat@shinshu-u.ac.jp.
RESUMEN / SUMMARY: - Transforming growth factor (TGF)-beta induces epithelial-mesenchymal transition (EMT) in pancreatic adenocarcinoma. In this study, we investigated how NADPH oxidase (Nox) 4-generated reactive oxygen species (ROS) regulate TGF-beta-induced EMT in pancreatic cancer cells. MATERIALS AND METHODS: Pancreatic cancer cells were transfected with Nox4 siRNAs or PTP1B mutants and subjected to TGF-beta-induced EMT assay. Expression of Nox4, TGF-beta, and N-cadherin was immunohistochemically-examined with patient tumor samples. RESULTS: Treatment of pancreatic cancer cells with TGF-beta induced Nox4 expression, indicating that Nox4 represents a major source for ROS production. The Nox4 inhibitor diphenylene iodonium and Nox4 siRNAs blocked TGF-beta-induced EMT phenotype including morphological changes, augmented migration, and altered expression of E-cadherin and Snail. Furthermore, PTP1B as a redox-sensor for Nox4-derived ROS participated in TGF-beta-promoted EMT. Nox4, TGF-beta, and N-cadherin were up-regulated in tumors from pancreatic cancer patients. CONCLUSIONS: These findings suggest that Nox4-derived ROS, at least in part, transmit TGF-beta-triggered EMT signals through PTP1B in pancreatic cancer.

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[116]

TÍTULO / TITLE: - Novel methylation biomarker panel for the early detection of pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Cancer Res. 2013 Dec 1;19(23):6544-55. doi: 10.1158/1078-0432.CCR-12-3224. Epub 2013 Oct 2.

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-12-3224

AUTORES / AUTHORS: - Yi JM; Guzzetta AA; Bailey VJ; Downing SR; Van Neste L; Chiappinelli KB; Keeley BP; Stark A; Herrera A; Wolfgang C; Pappou EP; Iacobuzio-Donahue CA; Goggins MG; Herman JG; Wang TH; Baylin SB; Ahuja N
INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of Oncology, Surgery, Urology, and Mechanic Engineering, Johns Hopkins University; Department of Biomedical Engineering, Johns Hopkins School of Medicine; Department of Pathology, The Sol Goldman Pancreatic Research Center, The Johns Hopkins Medical Institutions, Baltimore, Maryland; MDxHealth, Ghent, Belgium; and Research Institute, Dongnam Institute of Radiological and Medical Sciences (DIRAMS), Busan, South Korea.
RESUMEN / SUMMARY: - PURPOSE: Pancreatic cancer is the fourth leading cause of cancer deaths and there currently is no reliable modality for the early detection of this disease. Here, we identify cancer-specific promoter DNA methylation of BNC1 and ADAMTS1 as a promising biomarker detection strategy meriting investigation in pancreatic cancer. EXPERIMENTAL DESIGN: We used a genome-wide pharmacologic transcriptome approach to identify novel cancer-specific DNA methylation alterations in pancreatic cancer cell lines. Of eight promising genes, we focused our studies on BNC1 and ADAMTS1 for further downstream analysis, including methylation and expression. We used a nanoparticle-enabled methylation on beads (MOB) technology to detect early-stage pancreatic cancers by analyzing DNA methylation in patient serum. RESULTS: We identified two novel genes, BNC1 (92%) and ADAMTS1 (68%), that showed a high frequency of methylation in pancreatic cancers (n = 143), up to 100% in PanIN-3 and 97% in stage I invasive cancers. Using the nanoparticle-enabled MOB technology, these alterations could be detected in serum samples (n = 42) from patients with pancreatic cancer, with a sensitivity for BNC1 of 79% [95% confidence interval (CI), 66%-91%] and for ADAMTS1 of 48% (95% CI, 33%-63%), whereas specificity was 89% for BNC1 (95% CI, 76%-100%) and 92% for ADAMTS1 (95% CI, 82%-100%). Overall sensitivity using both markers is 81% (95% CI, 69%-93%) and specificity is 85% (95% CI, 71%-99%). CONCLUSIONS: Promoter DNA methylation of BNC1 and ADAMTS1 is a potential biomarker to detect early-stage pancreatic cancers. Assaying the promoter methylation status of these genes in circulating DNA from serum is a promising strategy for early detection of pancreatic cancer and has the potential to improve mortality from this disease. Clin Cancer Res; 19(23); 6544-55. ©2013 AACR.

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[117]
TÍTULO / TITLE: - HAb18G/CD147 Promotes pSTAT3-Mediated Pancreatic Cancer Development via CD44s.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 22.

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-0621

AUTORES / AUTHORS: - Li L; Tang W; Wu X; Karnak D; Meng X; Thompson R; Hao X; Li Y; Qiao XT; Lin J; Fuchs J; Simeone DM; Chen ZN; Lawrence TS; Xu L

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of Radiation Oncology and Surgery, University of Michigan Medical Center; Department of Cell and Developmental Biology, University of Michigan, Ann Arbor, Michigan; Cell Engineering Research Centre and Department of Cell Biology, State Key Laboratory of Cancer Biology, Fourth Military Medical University, Xi'an; Department of Hematology/Oncology, Hainan University Medical School, Haikou, Hainan, China; Departments of Molecular Biosciences and Radiation Oncology, University of Kansas, Lawrence, Kansas; Department of Pediatrics, College of Medicine; and Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, Ohio State University, Columbus, Ohio.

RESUMEN / SUMMARY: - PURPOSE: Signal transducer and activator of transcription 3 (STAT3) plays a critical role in initiation and progression of pancreatic cancer. However, therapeutically targeting STAT3 has failed clinically. We previously identified HAb18G/CD147 as an effective target for cancer treatment. In this study, we aimed to investigate the potential role of HAb18G/CD147 in STAT3-involved pancreatic tumorigenesis in vitro and in vivo.EXPERIMENTAL DESIGN: The expression of HAb18G/CD147, pSTAT3, and CD44s was determined in tissue microarrays. The tumorigenic function and molecular signaling mechanism of HAb18G/CD147 were assessed by in vitro cellular and clonogenic growth, reporter assay, immunoblot assay, immunofluorescence staining, immunoprecipitation, and in vivo tumor formation using loss or gain-of-function strategies.RESULTS: Highly expressed HAb18G/CD147 promoted cellular and clonogenic growth in vitro and tumorigenicity in vivo. Cyclophilin A (CyPA), a ligand of CD147, stimulated STAT3 phosphorylation and its downstream genes cyclin D1/survivin through HAb18G/CD147-dependent mechanisms. HAb18G/CD147 was associated and colocalized with cancer stem cell marker CD44s in lipid rafts. The inhibitors of STAT3 and survivin, as well as CD44s neutralizing antibodies suppressed the HAb18G/CD147-induced cell growth. High HAb18G/CD147 expression in pancreatic cancer was significantly correlated with the poor tumor differentiation, and the high coexpression of HAb18G/CD147-CD44s-STAT3 associated with poor survival of patients with pancreatic cancer.CONCLUSIONS: We identified HAb18G/CD147 as a novel upstream activator of STAT3, which interacts with CD44s and plays a critical role in the development of pancreatic cancer. The data suggest that HAb18G/CD147 could be a promising therapeutic target for highly aggressive pancreatic cancer and a surrogate marker in the STAT3-targeted molecular therapies. Clin Cancer Res; 1-13. ©2013 AACR.

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[118]

TÍTULO / TITLE: - Par-4 downregulation confers cisplatin resistance in pancreatic cancer cells via PI3K/Akt pathway-dependent EMT.

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

REVISTA / JOURNAL: - Toxicol Lett. 2013 Oct 19;224(1):7-15. doi: 10.1016/j.toxlet.2013.10.008.

●● Enlace al texto completo (gratuito o de pago) 1016/j.toxlet.2013.10.008

AUTORES / AUTHORS: - Tan J; You Y; Xu T; Yu P; Wu D; Deng H; Zhang Y; Bie P

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, First Affiliated Hospital, Third Military Medical University, Chongqing 400038, PR China.

RESUMEN / SUMMARY: - Cisplatin (CDDP) efficiency in pancreatic cancer therapy is limited due to development of drug resistance. However, the comprehensive mechanisms remain largely unclear. In this study, we first established a CDDP-resistant pancreatic cancer cell line-BXPC-3/CDDP from its parental cell line-BXPC-3. The results showed that CDDP resistance in BXPC-3/CDDP cells correlates with changes in cellular EMT phenotypes. Prostate apoptosis response-4 (Par-4) expression at both mRNA and protein levels were reduced in CDDP-resistant BXPC-3/CDDP cells compared with that in BXPC-3 cells. Ectopic expression of Par-4 reversed EMT and CDDP resistance in BXPC-3/CDDP cells. In BXPC-3 cells, knockdown of Par-4 expression induces EMT and CDDP insensitivity, however, these effects were blocked by inhibition of PI3K/Akt pathway using LY294002. Furthermore, Par-4 knockdown could significantly stimulate PI3K/Akt signaling in BXPC-3 cells. In vivo studies, xenograft BXPC-3 tumors were sensitive to CDDP treatment. Treatment with CDDP alone had little effect on the growth of Par-4 siRNA-transfected BXPC-3 tumors in nude mice and the survival rate compared with control. Inhibition of PI3K/Akt pathway using LY294002 reversed CDDP resistance in Par-4 siRNA-transfected BXPC-3 tumors. In conclusion, these results indicate that Par-4 downregulation confers CDDP resistance via PI3K/Akt pathway-dependent EMT in BXPC-3 cells. Therefore, Par-4 may be a potential target for overcoming CDDP resistance in pancreatic cancer.

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[119]

TÍTULO / TITLE: - Apigenin potentiates the growth inhibitory effects by IKK-beta-mediated NF-kappaB activation in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Toxicol Lett. 2013 Oct 19;224(1):157-164. doi: 10.1016/j.toxlet.2013.10.007.

●● Enlace al texto completo (gratuito o de pago) 1016/j.toxlet.2013.10.007

AUTORES / AUTHORS: - Wu DG; Yu P; Li JW; Jiang P; Sun J; Wang HZ; Zhang LD; Wen MB; Bie P

INSTITUCIÓN / INSTITUTION: - Institute of Hepatobiliary Surgery, Southwest Hospital, Third Military Medical University, Chongqing 400038, China.

RESUMEN / SUMMARY: - Apigenin is a potential chemopreventive agent for cancer prevention. Because of the central role of transcription factor nuclear factor-kappaB (NF-kappaB) in pancreatic cancer, we investigated the roles of NF-kappaB in apigenin-induced growth inhibition in pancreatic cancer cells. It showed that apigenin reduced cell growth and induced apoptosis in the cells. Apigenin treatment down-regulated not only basal but also TNF-alpha-induced NF-kappaB DNA binding activity, NF-kappaB transcription activity, inhibitor of kappaB (IkappaB)-alpha phosphorylation together with translocation of p65 and p50, and it accompanied with the blockade of IkappaB kinase (IKK)-beta activity. Moreover, IKK blockage potentiated the anticancer efficacy of apigenin and IKK-beta overexpression attenuated the apigenin-induced cell growth inhibition. Additionally, apigenin (30mg/kg) administration suppressed pancreatic cancer growth and IKK-beta activation in nude mice xenograft. These results indicated that apigenin had a potential to inhibit IKK-beta-mediated NF-kappaB activation, and was a valuable agent for the pancreatic cancer treatment.

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[120]

TÍTULO / TITLE: - Pancreatitis Before Pancreatic Cancer: Clinical Features and Influence on Outcome.

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

REVISTA / JOURNAL: - J Clin Gastroenterol. 2013 Oct 22.

●● Enlace al texto completo (gratuito o de pago)

1097/MCG.0b013e3182a9f879

AUTORES / AUTHORS: - Dzeletovic I; Harrison ME; Crowell MD; Pannala R; Nguyen CC; Wu Q; Faigel DO

INSTITUCIÓN / INSTITUTION: - Divisions of *Gastroenterology daggerHepatology double daggerHealth Sciences Research, Mayo Clinic, Scottsdale, AZ.

RESUMEN / SUMMARY: - OBJECTIVES:: Pancreatitis is considered a possible risk factor for and a presentation of pancreatic adenocarcinoma (PA). We aimed to evaluate a large PA patient registry to determine whether prior history of pancreatitis influenced survival. METHODS:: We retrospectively analyzed the Mayo Clinic Biospecimen Resource for Pancreas Research database from January 1992 to September 2011. Data collected included demographic characteristics, history of tobacco or alcohol use, diabetes mellitus (DM), cholelithiasis, pseudocyst, and details regarding PA. Clinical characteristics and outcomes of PA patients with pancreatitis were compared with PA patients without pancreatitis history. RESULTS:: We analyzed 2573 patients with PA diagnosis. Among these patients, 195 (8%) were identified who had pancreatitis diagnosis >/=10 days before PA diagnosis. The cohort with pancreatitis history included more patients with DM (30% vs. 18%; P<0.001) and more smokers (68% vs. 58%; P=0.02). Compared with patients without pancreatitis history, these patients received diagnoses of PA at a younger age (63 vs. 65 y; P=0.005) and earlier stage (stages I and II; 52% vs. 37%; P<0.001). A greater percentage had history of surgery with curative intent (50% vs. 43%; P=0.001) and significantly better survival [median (range), 387 d (314 to 460 d) vs. 325 d (306 to 344 d); P=0.003]. CONCLUSIONS:: Patients with PA and pancreatitis had more weight loss and DM, but had PA diagnosis at an earlier stage, were more likely to have pancreatic surgery, and therefore better survival than PA patients without pancreatitis, likely due to the earlier diagnosis. Further studies are needed to evaluate whether screening for PA in patients with pancreatitis history would provide survival benefit.

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[121]

TÍTULO / TITLE: - Antiprotease Strategy in Pancreatic Cancer Treatment: Emergences From a Preclinical Study.

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

REVISTA / JOURNAL: - Pancreas. 2013 Nov 6.

●● Enlace al texto completo (gratuito o de pago)

1097/MPA.0b013e3182a6486e

AUTORES / AUTHORS: - Brandi G; Tavolari S; Guarnieri T; Di Marco M; Paterini P; Macchini M; Di Girolamo S; Papi A; De Rosa F; Biasco G

INSTITUCIÓN / INSTITUTION: - From the *Department of Experimental, Diagnostic and Specialty Medicine, dagger"G. Prodi" Interdepartmental Center for Cancer Research

(C.I.R.C.), and double daggerCenter for Applied Biomedical Research (C.R.B.A.), S. Orsola-Malpighi University Hospital; section signDepartment of Biological, Geological and Environmental Sciences; and parallelDepartment of Medical and Surgical Sciences, S. Orsola-Malpighi University Hospital, Bologna, Italy.

RESUMEN / SUMMARY: - OBJECTIVES: Resistance to gemcitabine is one of the main causes of treatment failure in pancreatic cancer. Compelling evidences have shown the involvement of nuclear factor kappaB (NF-kappaB) activation in such phenomenon. The protease inhibitor gabexate mesilate has been shown to inhibit NF-kappaB. We here investigated if combined treatment with this drug could improve gemcitabine antitumoral efficacy in pancreatic cancer cells. METHODS: The effect of gabexate mesilate and gemcitabine, both used at concentrations achievable in human plasma, was assessed on in vitro pancreatic cancer cell growth, invasion, and tumor angiogenesis. The molecular mechanism at the basis of these effects was also investigated. RESULTS: Gabexate mesilate significantly increased gemcitabine anti-invasive and antiangiogenic efficacy. This effect was related to inhibition of gemcitabine-induced NF-kappaB activation by gabexate mesilate, which prevented RelA/p65 nuclear translocation and resulted in metalloproteinase 2, metalloproteinase 9, vascular endothelial growth factor, and interleukin 8 down-regulation. Combined treatment with gabexate mesilate also inhibited gemcitabine-induced extracellular-regulated kinase ½ and AKT activation by increased expression of Raf kinase inhibitor protein and phosphatase and tensin homolog. CONCLUSIONS: Combined treatment with gabexate mesilate sensitizes pancreatic cancer cells to gemcitabine by inhibition of the NF-kappaB pathway. The efficacy of this therapeutic strategy in pancreatic cancer patients remains to be established and deserves future clinical investigation.

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[122]

TÍTULO / TITLE: - A new endoscopic ultrasonography image processing method to evaluate the prognosis for pancreatic cancer treated with interstitial brachytherapy.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Oct 14;19(38):6479-84. doi: 10.3748/wjg.v19.i38.6479.

●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i38.6479

AUTORES / AUTHORS: - Xu W; Liu Y; Lu Z; Jin ZD; Hu YH; Yu JG; Li ZS

INSTITUCIÓN / INSTITUTION: - Wei Xu, Zheng Lu, Zhen-Dong Jin, Yu-Hong Hu, Zhao-Shen Li, Department of Gastroenterology, Changhai Hospital, Second Military Medical University, Shanghai 200433, China.

RESUMEN / SUMMARY: - AIM: To develop a fuzzy classification method to score the texture features of pancreatic cancer in endoscopic ultrasonography (EUS) images and evaluate its utility in making prognosis judgments for patients with unresectable pancreatic cancer treated by EUS-guided interstitial brachytherapy. METHODS: EUS images from our retrospective database were analyzed. The regions of interest were drawn, and texture features were extracted, selected, and scored with a fuzzy classification method using a C++ program. Then, patients with unresectable pancreatic cancer were enrolled to receive EUS-guided iodine 125 radioactive seed implantation. Their fuzzy classification scores, tumor volumes, and carbohydrate antigen 199 (CA199) levels before and after the brachytherapy were recorded. The association between the changes in these parameters and overall survival was

analyzed statistically. RESULTS: EUS images of 153 patients with pancreatic cancer and 63 non-cancer patients were analyzed. A total of 25 consecutive patients were enrolled, and they tolerated the brachytherapy well without any complications. There was a correlation between the change in the fuzzy classification score and overall survival (Spearman test, r = 0.616, P = 0.001), whereas no correlation was found to be significant between the change in tumor volume (P = 0.663), CA199 level (P = 0.659), and overall survival. There were 15 patients with a decrease in their fuzzy classification score after brachytherapy, whereas the fuzzy classification score increased in another 10 patients. There was a significant difference in overall survival between the two groups (67 d vs 151 d, P = 0.001), but not in the change of tumor volume and CA199 level. CONCLUSION: Using the fuzzy classification method to analyze EUS images of pancreatic cancer is feasible, and the method can be used to make prognosis judgments for patients with unresectable pancreatic cancer treated by interstitial brachytherapy.

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[123]
TÍTULO / TITLE: - The carboxyl terminus and pore-forming domain properties specific to Cx37 are necessary for Cx37 mediated suppression of insulinoma cell proliferation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Am J Physiol Cell Physiol. 2013 Oct 16.
●● Enlace al texto completo (gratuito o de pago) 1152/ajpcell.00159.2013
AUTORES / AUTHORS: - Nelson TK; Sorgen PL; Burt JM
INSTITUCIÓN / INSTITUTION: - University of Arizona.
RESUMEN / SUMMARY: - Connexin 37 (Cx37) suppresses cell proliferation when expressed in rat insulinoma (Rin) cells, an effect also manifest in vivo during vascular development and in response to tissue injury. Mutant forms of Cx37 with non-functional channels but normally localized, wild-type carboxyl termini are not growth suppressive. Here we determined whether the carboxyl terminal (CT) domain is required for Cx37-mediated growth suppression and whether the Cx37 pore-forming domain can be replaced with the Cx43 pore-forming domain and still retain growth suppressive properties. We show that despite forming functional gap junction channels and hemichannels, Cx37 with residues subsequent to 273 replaced with a V5-epitope tag (Cx37-273tr*V5) had no effect on the proliferation of Rin cells, did not facilitate G1 cell cycle arrest with serum deprivation, and did not prolong cell cycle time comparably to the wild-type protein. The chimera Cx43*CT37, comprising the pore forming domain of Cx43 and CT of Cx37, also did not suppress proliferation, despite forming functional gap junctions with a permselective profile similar to wild-type Cx37. Differences in channel behavior of both Cx37-273tr*V5 and Cx43*CT37 relative to their wild-type counterparts and failure of the Cx37-CT to interact as the Cx43-CT does with the Cx43 cytoplasmic loop suggest that the Cx37-CT and pore-forming domains are both essential to growth suppression by Cx37.

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[124]
TÍTULO / TITLE: - A pilot study of in vivo identification of pancreatic cystic neoplasms with needle-based confocal laser endomicroscopy under endosonographic guidance.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Endoscopy. 2013 Dec;45(12):1006-13. doi: 10.1055/s-0033-1344714. Epub 2013 Oct 25.

●● Enlace al texto completo (gratuito o de pago) 1055/s-0033-1344714

AUTORES / AUTHORS: - Konda VJ; Meining A; Jamil LH; Giovannini M; Hwang JH; Wallace MB; Chang KJ; Siddiqui UD; Hart J; Lo SK; Saunders MD; Aslanian HR; Wroblewski K; Waxman I

INSTITUCIÓN / INSTITUTION: - Center for Endoscopic Research and Therapeutics, Section of Gastroenterology, University of Chicago Medicine, Chicago, Illinois, USA.

RESUMEN / SUMMARY: - Background and study aims: Endoscopic ultrasound (EUS) with fine-needle aspiration (FNA) of pancreatic cystic lesions (PCL) is flawed by inadequate diagnostic yield. Needle-based confocal laser endomicroscopy (nCLE) utilizes a sub-millimeter probe that is compatible with an EUS needle and enables real-time imaging with microscopic detail of PCL. The aims of the In vivo nCLE Study in the Pancreas with Endosonography of Cystic Tumors (INSPECT) pilot study were to assess both the diagnostic potential of nCLE in differentiating cyst types and the safety of the technique. Patients and methods: Eight referral centers performed nCLE in patients with PCL. Stage 1 defined descriptive terms for structures visualized by an off-line, unblinded consensus review. Cases were reviewed with a gastrointestinal pathologist to identify correlations between histology and nCLE. Stage 2 assessed whether the specific criteria defined in Stage 1 could identify pancreatic cystic neoplasms (PCN) including intraductal papillary mucinous neoplasms, mucinous cystic adenoma, or adenocarcinoma in an off-line blinded consensus review. Results: A total of 66 patients underwent nCLE imaging and images were available for 65, 8 of which were subsequently excluded due to insufficient information for consensus reference diagnosis. The presence of epithelial villous structures based on nCLE was associated with PCN (P = 0.004) and provided a sensitivity of 59 %, specificity of 100 %, positive predictive value of 100 %, and negative predictive value of 50 %. The overall complication rate was 9 % and included pancreatitis (1 mild case, 1 moderate case), transient abdominal pain (n = 1), and intracystic bleeding not requiring any further measures (n = 3). Conclusions: These preliminary data suggested that nCLE has a high specificity in the detection of PCN, but may be limited by a low sensitivity. The safety of nCLE requires further evaluation.

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[125]

TÍTULO / TITLE: - L-Methionine inhibits growth of human pancreatic cancer cells.

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

REVISTA / JOURNAL: - Anticancer Drugs. 2013 Oct 11.

●● Enlace al texto completo (gratuito o de pago) 1097/CAD.0000000000000038

AUTORES / AUTHORS: - Benavides MA; Bosland MC; da Silva CP; Gomes Sares CT; Cerqueira de Oliveira AM; Kemp R; Dos Reis RB; Martins VR; Sampaio SV; Bland KI; Grizzle WE; Dos Santos JS

INSTITUCIÓN / INSTITUTION: - Departments of aSurgery bPharmacology, University of Sao Paulo-Ribeirao Preto, Sao Paulo, Brazil cDepartment of Pathology, College of Medicine, University of Illinois at Chicago, Chicago, Illinois Departments of dSurgery ePathology, College of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA.

RESUMEN / SUMMARY: - We have previously shown that L-methionine inhibits proliferation of breast, prostate, and colon cancer cells. This study extends these findings to BXPC-3 (mutated p53) and HPAC (wild-type p53) pancreatic cancer cells and explores the reversibility of these effects. Cells were exposed to L-methionine (5 mg/ml) for 7 days or for 3 days, followed by 4 days of culture without L-methionine (recovery). Cell proliferation, apoptosis, and cell cycle effects were assessed by flow cytometry after staining for Ki-67 or annexin V/propidium iodide. Cell proliferation was reduced by 31-35% after 7 days of methionine exposure; the effect persisted in BXPC-3 and HPAC cells after 4 days of recovery. Methionine increased apoptosis by 40-75% in HPAC cells, but not in BXPC-3 cells. Continuous exposure to methionine caused accumulation of BXPC-3 cells in the S phase and HPAC cells in both the G0/G1 and S phases; however, after 4 days of recovery, these effects disappeared. In conclusion, L-methionine inhibits proliferation and interferes with the cell cycle of BXPC-3 and HPAC pancreatic cancer cells; the effects on apoptosis remarkably persisted after methionine withdrawal. Apoptosis was induced only in BXPC-3 cells. Some of the differences in the effects of methionine between cell lines may be related to disparate p53 status. These findings warrant further studies on the potential therapeutic benefit of L-methionine against pancreatic cancer.

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[126]
TÍTULO / TITLE: - The stromal compartments in pancreatic cancer: Are there any therapeutic targets?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cancer Lett. 2013 Oct 16. pii: S0304-3835(13)00708-8. doi: 10.1016/j.canlet.2013.09.039.
●● Enlace al texto completo (gratuito o de pago) 1016/j.canlet.2013.09.039
AUTORES / AUTHORS: - Lunardi S; Muschel RJ; Brunner TB
INSTITUCIÓN / INSTITUTION: - Gray Institute for Radiation Oncology and Biology, Department of Oncology, University of Oxford, Churchill Hospital, RRI, Oxford OX3 7LJ, UK.
RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is characterised by an abundant stromal response also known as a desmoplastic reaction. Pancreatic Stellate Cells have been identified as playing a key role in pancreatic cancer desmoplasia. There is accumulating evidence that the stroma contributes to tumour progression and to the low therapeutic response of PDAC patients. In this review we described the main actors of the desmoplastic reaction within PDAC and novel therapeutic approaches that are being tested to block the detrimental function of the stroma.

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[127]
TÍTULO / TITLE: - Prediction of Malignancy in Cystic Neoplasms of the Pancreas: A Population-Based Cohort Study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Am J Gastroenterol. 2013 Oct 1. doi: 10.1038/ajg.2013.334.
●● Enlace al texto completo (gratuito o de pago) 1038/ajg.2013.334

AUTORES / AUTHORS: - Wu BU; Sampath K; Berberian CE; Kwok KK; Lim BS; Kao KT; Giap AQ; Kosco AE; Akmal YM; Difronzo AL; Yu W; Ngor EW

INSTITUCIÓN / INSTITUTION: - 1] Center for Pancreatic Care, Southern California Permanente Medical Group, Kaiser Permanente Los Angeles Medical Center, Los Angeles, California, USA [2] Department of Gastroenterology, Kaiser Permanente Los Angeles Medical Center, Los Angeles, California, USA.

RESUMEN / SUMMARY: - OBJECTIVES:Pancreatic cystic neoplasms (PCNs) are being detected with increased frequency. The aims of this study were to determine the incidence of malignancy and develop an imaging-based system for prediction of malignancy in PCN.METHODS:We conducted a retrospective cohort study of patients >/=18 years of age with confirmed PCN from January 2005 to December 2010 in a community-based integrated care setting in Southern California. Patients with history of acute or chronic pancreatitis were excluded. Malignancy diagnosed within 3 months of cyst diagnosis was considered as pre-existing. Subsequent incidence of malignancy during surveillance was calculated based on person-time at risk. Age- and gender-adjusted standardized incidence ratio (SIR) was calculated with the non-cyst reference population. Recursive partitioning was used to develop a risk prediction model based on cyst imaging features.RESULTS:We identified 1,815 patients with confirmed PCN. A total of 53 (2.9%) of patients were diagnosed with cyst-related malignancy during the study period. The surveillance cohort consisted of 1,735 patients with median follow-up of 23.4 months. Incidence of malignancy was 0.4% per year during surveillance. The overall age- and gender-adjusted SIR for pancreatic malignancy was 35.0 (95% confidence level 26.6, 46.0). Using recursive partitioning, we stratified patients into low (<1%), intermediate (1-5%), and high (9-14%) risk of harboring malignant PCN based on four cross-sectional imaging features: size, pancreatic duct dilatation, septations with calcification as well as growth. Area under the receiver operator characteristic curve for the prediction model was 0.822 (training) and 0.808 (testing).CONCLUSIONS:Risk of pancreatic malignancy was lower than previous reports from surgical series but was still significantly higher than the reference population. A risk stratification system based on established imaging criteria may help guide future management decisions for patients with PCN.Am J Gastroenterol advance online publication, 1 October 2013; doi:10.1038/ajg.2013.334.

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[128]

TÍTULO / TITLE: - Acinar cell cystadenoma of the pancreas: a benign neoplasm or non-neoplastic ballooning of acinar and ductal epithelium?

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

REVISTA / JOURNAL: - Am J Surg Pathol. 2013 Sep;37(9):1329-35. doi: 10.1097/PAS.0b013e3182a1ad72.

●● Enlace al texto completo (gratuito o de pago)

1097/PAS.0b013e3182a1ad72

AUTORES / AUTHORS: - Singhi AD; Norwood S; Liu TC; Sharma R; Wolfgang CL; Schulick RD; Zeh HJ; Hruban RH

INSTITUCIÓN / INSTITUTION: - Departments of *Pathology parallelSurgery, University of Pittsburgh Medical Center, Pittsburgh, PA Departments of daggerPathology double daggerOncology section signSurgery, The Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins University School of Medicine, Baltimore, MD.

RESUMEN / SUMMARY: - Acinar cell cystadenoma (ACA) of the pancreas was initially described as a non-neoplastic cyst of the pancreas and, at that time, referred to as “acinar cystic transformation.” In subsequent studies, these lesions were given the designation of “-oma,” despite the relative lack of evidence supporting a neoplastic process. To characterize these lesions further, we examined the clinical, pathologic, and immunohistochemical features of 8 ACAs. The majority of patients were female (7 of 8, 88%) and ranged in age from 18 to 57 years (mean, 43 y). Grossly, the cysts involved the head (n=5), body (n=1), or the entire pancreas (n=2). ACAs were either multilocular (n=4) or unilocular (n=4) and ranged in size from 1.8 to 15 cm (mean, 6.8 cm). Histologically, multilocular ACAs were lined by patches of acinar and ductal epithelium. Immunolabeling, including double-labeling for cytokeratin 19 and chymotrypsin, highlighted the patchy pattern of the ductal and acinar cells lining the cysts. In some areas, the cysts with patches of acinar and ductal differentiation formed larger locules with incomplete septa as they appeared to fuse with other cysts. In contrast, the unilocular cases were lined by 1 to 2 cell layers of acinar cells with little intervening ductal epithelium. Nuclear atypia, mitotic figures, necrosis, infiltrative growth, and associated invasive carcinoma were absent in all cases. In addition, we assessed the clonal versus polyclonal nature of ACAs, occurring in women, using X-chromosome inactivation analysis of the human androgen receptor (AR) gene. Five of 7 cases were informative and demonstrated a random X-chromosome inactivation pattern. Clinical follow-up information was available for all patients, and follow-up ranged from 10 months to 7.8 years (mean, 3.6 y), with no evidence of recurrence or malignant transformation. We hypothesize that early lesions are marked by acinar dilatation that expands into and incorporates smaller ductules and later larger ducts. As the cysts increase in size, they fuse forming larger cysts. Later lesions demonstrate a unilocular cyst lined by predominantly acinar epithelium with scattered ductal cells. The term cystadenoma, with its neoplastic connotation, does not seem to accurately reflect the histologic, immunohistochemical, or molecular features of these lesions. We suggest readopting the term “acinar cystic transformation” until the non-neoplastic versus neoplastic origin of these lesions can be resolved.

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[129]

TÍTULO / TITLE: - Differential gene expression of the key signalling pathway in para-carcinoma, carcinoma and relapse human pancreatic cancer.

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

REVISTA / JOURNAL: - Cell Biochem Funct. 2013 Oct 3. doi: 10.1002/cbf.3009.

●● Enlace al texto completo (gratuito o de pago) 1002/cbf.3009

AUTORES / AUTHORS: - Chang ZY; Sun R; Ma YS; Fu D; Lai XL; Li YS; Wang XH; Zhang XP; Lv ZW; Cong XL; Li WP

INSTITUCIÓN / INSTITUTION: - Veterinary Faculty, College of Veterinary Medicine, Hunan Agricultural University, Changsha, China.

RESUMEN / SUMMARY: - Pancreatic cancer (PC) has a high rate of mortality and a poorly understood mechanism of progression. Investigation of the molecular mechanism of PC and exploration of the specific markers for early diagnosis and specific targets of therapy are key points to prevent and treat PC effectively and to improve their prognosis. In our study, expression profiles experiment of para-carcinoma, carcinoma and relapse human PC was performed using Agilent human

whole genomic oligonucleotide microarrays with 45 000 probes. Differentially expressed genes related with PC were screened and analysed further by Gene Ontology term analysis and Kyoto encyclopaedia of genes and genomes pathway analysis. Our results showed that there were 3853 differentially expressed genes associated with pancreatic carcinogenesis and relapse. In addition, our study found that PC was related to the Jak-STAT signalling pathway, PPAR signalling pathway and Calcium signalling pathway, indicating their potential roles in pancreatic carcinogenesis and progress. Copyright © 2013 John Wiley & Sons, Ltd.

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[130]
TÍTULO / TITLE: - A selective mitochondrial-targeted chlorambucil with remarkable cytotoxicity in breast and pancreatic cancers.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Med Chem. 2013 Nov 27;56(22):9170-9. doi: 10.1021/jm4012438. Epub 2013 Nov 7.
●● Enlace al texto completo (gratuito o de pago) 1021/jm4012438
AUTORES / AUTHORS: - Millard M; Gallagher JD; Olenyuk BZ; Neamati N
INSTITUCIÓN / INSTITUTION: - Department of Pharmacology and Pharmaceutical Sciences, School of Pharmacy, University of Southern California , 1985 Zonal Avenue, Los Angeles, California 90089, United States.
RESUMEN / SUMMARY: - Nitrogen mustards, widely used as chemotherapeutics, have limited safety and efficacy. Mitochondria lack a functional nucleotide excision repair mechanism to repair DNA adducts and are sensitive to alkylating agents. Importantly, cancer cells have higher intrinsic mitochondrial membrane potential (Deltapsimt) than normal cells. Therefore, selectively targeting nitrogen mustards to cancer cell mitochondria based on Deltapsimt could overcome those limitations. Herein, we describe the design, synthesis, and evaluation of Mito-Chlor, a triphenylphosphonium derivative of the nitrogen mustard chlorambucil. We show that Mito-Chlor localizes to cancer cell mitochondria where it acts on mtDNA to arrest cell cycle and induce cell death, resulting in a 80-fold enhancement of cell kill in a panel of breast and pancreatic cancer cell lines that are insensitive to the parent drug. Significantly, Mito-Chlor delayed tumor progression in a mouse xenograft model of human pancreatic cancer. This is a first example of repurposing chlorambucil, a drug not used in breast and pancreatic cancer treatment, as a novel drug candidate for these diseases.

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[131]
TÍTULO / TITLE: - Liver cancer presenting as a pancreatic mass.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Gastrointest Endosc. 2013 Nov 22. pii: S0016-5107(13)02447-4. doi: 10.1016/j.gie.2013.10.016.
●● Enlace al texto completo (gratuito o de pago) 1016/j.gie.2013.10.016
AUTORES / AUTHORS: - Ghaoui R; Gonzalez M; Desilets DJ
INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology, Department of Medicine.

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[132]

TÍTULO / TITLE: - Magnetic resonance imaging of cystic pancreatic lesions in adults: an update in current diagnostic features and management.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Abdom Imaging. 2013 Nov 22.
●● Enlace al texto completo (gratuito o de pago) 1007/s00261-013-0048-y
AUTORES / AUTHORS: - Barral M; Soyer P; Dohan A; Laurent V; Hoeffel C; Fishman EK; Boudiaf M
INSTITUCIÓN / INSTITUTION: - Department of Abdominal Imaging, Hopital Lariboisiere-APHP and Universite Diderot-Paris 7, 2, rue Ambroise Pare, 75010, Paris, France, matthias_barral@yahoo.fr.
RESUMEN / SUMMARY: - Magnetic resonance (MR) imaging has become a widespread diagnostic solving tool for the detection and characterization of a large range of pancreatic cystic lesions. Benign and malignant cystic lesions of the pancreas including serous microcystic adenoma, mucinous cystic tumor, intraductal papillary mucinous tumor, solid pseudopapillary tumor, and also the less common lesions such as cystic endocrine tumors, cystic metastases, and lymphangiomas have suggestive MR imaging presentation that allows them to be differentiated from each other. Knowledge of MR imaging findings of cystic pancreatic lesions is critical to help suggest the diagnosis and chose the best therapeutic approach. The purpose of this review is to discuss and illustrate MR imaging features that are helpful for pancreatic cystic lesion detection and characterization and to provide an update in current MR imaging diagnostic features and management.

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[133]
TÍTULO / TITLE: - Hypofractionated Image-Guided IMRT in Advanced Pancreatic Cancer With Simultaneous Integrated Boost to Infiltrated Vessels Concomitant With Capecitabine: A Phase I Study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Dec 1;87(5):1000-6. doi: 10.1016/j.ijrobp.2013.09.012.
●● Enlace al texto completo (gratuito o de pago) 1016/j.ijrobp.2013.09.012
AUTORES / AUTHORS: - Passoni P; Reni M; Cattaneo GM; Slim N; Cereda S; Balzano G; Castoldi R; Longobardi B; Bettinardi V; Gianolli L; Gusmini S; Staudacher C; Calandrino R; Di Muzio N
INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, San Raffaele Scientific Institute, Milan, Italy. Electronic address: passoni.paolo@hsr.it.
RESUMEN / SUMMARY: - PURPOSE: To determine the maximum tolerated radiation dose (MTD) of an integrated boost to the tumor subvolume infiltrating vessels, delivered simultaneously with radical dose to the whole tumor and concomitant capecitabine in patients with pretreated advanced pancreatic adenocarcinoma. METHODS AND MATERIALS: Patients with stage III or IV pancreatic adenocarcinoma without progressive disease after induction chemotherapy were eligible. Patients underwent simulated contrast-enhanced four-dimensional computed tomography and fluorodeoxyglucose-labeled positron emission tomography. Gross tumor volume 1 (GTV1), the tumor, and GTV2, the tumor subvolume 1 cm around the infiltrated vessels, were contoured. GTVs were fused to generate Internal Target Volume (ITV)1 and ITV2. Biological tumor volume (BTV) was fused with ITV1 to create the

BTV+Internal Target Volume (ITV) 1. A margin of 5/5/7 mm (7 mm in cranium-caudal) was added to BTV+ITV1 and to ITV2 to create Planning Target Volume (PTV) 1 and PTV2, respectively. Radiation therapy was delivered with tomotherapy. PTV1 received a fixed dose of 44.25 Gy in 15 fractions, and PTV2 received a dose escalation from 48 to 58 Gy as simultaneous integrated boost (SIB) in consecutive groups of at least 3 patients. Concomitant chemotherapy was capecitabine, 1250 mg/m(2) daily. Dose-limiting toxicity (DLT) was defined as any treatment-related G3 nonhematological or G4 hematological toxicity occurring during the treatment or within 90 days from its completion. RESULTS: From June 2005 to February 2010, 25 patients were enrolled. The dose escalation on the SIB was stopped at 58 Gy without reaching the MTD. One patient in the 2(nd) dose level (50 Gy) had a DLT: G3 acute gastric ulcer. Three patients had G3 late adverse effects associated with gastric and/or duodenal mucosal damage. All patients received the planned dose of radiation. CONCLUSIONS: A dose of 44.25 Gy in 15 fractions to the whole tumor with an SIB of 58 Gy to small tumor subvolumes concomitant with capecitabine is feasible in chemotherapy-pretreated patients with advanced pancreatic cancer.

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[134]

TÍTULO / TITLE: - Mapping patterns of local recurrence after pancreaticoduodenectomy for pancreatic adenocarcinoma: a new approach to adjuvant radiation field design.

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

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Dec 1;87(5):1007-15. doi: 10.1016/j.ijrobp.2013.09.005.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ijrobp.2013.09.005

AUTORES / AUTHORS: - Dholakia AS; Kumar R; Raman SP; Moore JA; Ellsworth S; McNutt T; Laheru DA; Jaffee E; Cameron JL; Tran PT; Hobbs RF; Wolfgang CL; Herman JM

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology & Molecular Radiation Sciences, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, Maryland.

RESUMEN / SUMMARY: - PURPOSE: To generate a map of local recurrences after pancreaticoduodenectomy (PD) for patients with resectable pancreatic ductal adenocarcinoma (PDA) and to model an adjuvant radiation therapy planning treatment volume (PTV) that encompasses a majority of local recurrences. METHODS AND MATERIALS: Consecutive patients with resectable PDA undergoing PD and 1 or more computed tomography (CT) scans more than 60 days after PD at our institution were reviewed. Patients were divided into 3 groups: no adjuvant treatment (NA), chemotherapy alone (CTA), or chemoradiation (CRT). Cross-sectional scans were centrally reviewed, and local recurrences were plotted to scale with respect to the celiac axis (CA), superior mesenteric artery (SMA), and renal veins on 1 CT scan of a template post-PD patient. An adjuvant clinical treatment volume comprising 90% of local failures based on standard expansions of the CA and SMA was created and simulated on 3 post-PD CT scans to assess the feasibility of this planning approach. RESULTS: Of the 202 patients in the study, 40 (20%), 34 (17%), and 128 (63%) received NA, CTA, and CRT adjuvant therapy, respectively. The rate of margin-positive resections was greater in CRT patients than in CTA patients (28% vs 9%, P=.023). Local recurrence occurred in 90 of the 202 patients overall (45%) and in 19 (48%), 22

(65%), and 49 (38%) in the NA, CTA, and CRT groups, respectively. Ninety percent of recurrences were within a 3.0-cm right-lateral, 2.0-cm left-lateral, 1.5-cm anterior, 1.0-cm posterior, 1.0-cm superior, and 2.0-cm inferior expansion of the combined CA and SMA contours. Three simulated radiation treatment plans using these expansions with adjustments to avoid nearby structures were created to demonstrate the use of this treatment volume. CONCLUSIONS: Modified PTVs targeting high-risk areas may improve local control while minimizing toxicities, allowing dose escalation with intensity-modulated or stereotactic body radiation therapy.

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[135]

TÍTULO / TITLE: - Myo-inositol trispyrophosphate-mediated hypoxia reversion controls pancreatic cancer in rodents and enhances gemcitabine efficacy.

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

REVISTA / JOURNAL: - Int J Cancer. 2013 Nov 10. doi: 10.1002/ijc.28597.

●● Enlace al texto completo (gratuito o de pago) 1002/ijc.28597

AUTORES / AUTHORS: - Raykov Z; Grekova SP; Bour G; Lehn JM; Giese NA; Nicolau C; Aprahamian M

INSTITUCIÓN / INSTITUTION: - German Cancer Research Center (DKFZ), Institut National pour la Sante et la Recherche Medicale, Unit 701, ImNeunheimerFeld 242, 69120, Heidelberg, Germany.

RESUMEN / SUMMARY: - Hypoxia and dysfunctional tumor vessels represent a prominent feature of pancreatic cancer, being, at least in part, responsible for chemotherapy resistance and immune suppression in these tumors. We tested whether the increase of oxygen delivery induced in vivo by myo-inositol trispyrophosphate (ITPP) can reverse hypoxia, control tumor growth and improve chemotherapy response. Tumor size, metastatic development (micro-CTscan follow up) and the survival of rats and nude or NOD.SCID mice, (bearing syngenic rat and MiaPaCa2- or patient-derived pancreatic tumors), were determined upon ITPP and/or gemcitabine treatment. Partial oxygen pressure, expression of angiogenic factors and tumor histology were evaluated. Infiltration and oxidative status of immune cells, as well as chemotherapy penetration in tumors, were determined by FACS, fluorometry, NO release assays, Western blot and confocal microscopy. Weekly intravenous ITPP application resulted in the inhibition of metastasis development and restricted primary tumor growth, showing a superior effect on the rats' survival compared to gemcitabine. ITPP treatment restored tumor normoxia and caused a reduction in HIF-1alpha levels, with subsequent VEGF and Lox downregulation, resulting in improved vessel structure and decreased desmoplasia. The latter effects translated into elevated immune cells influx and improved susceptibility to gemcitabine treatment. Growth of human pancreatic tumor xenografts was strongly inhibited by administration of ITPP. ITPP exploits a two-stage mechanism causing rapid, early, and sustainable late stage normoxia. This is due to angiogenic factor modulation and vascular normalization, leading to enhanced chemotherapy delivery and synergistic life prolongation, upon combination with low doses of gemcitabine. © 2013 Wiley Periodicals, Inc.

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[136]

TÍTULO / TITLE: - Effect of combined treatment with recombinant interleukin-2 and allicin on pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Mol Biol Rep. 2013 Dec;40(12):6579-85. doi: 10.1007/s11033-013-2766-1. Epub 2013 Oct 18.
●● Enlace al texto completo (gratuito o de pago) 1007/s11033-013-2766-1
AUTORES / AUTHORS: - Wang CJ; Wang C; Han J; Wang YK; Tang L; Shen DW; Zhao Y; Xu RH; Zhang H
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Shanghai East Hospital, Tongji University School of Medicine, No.150 Jimo Road, Pudong New District, Shanghai, 200120, China.
RESUMEN / SUMMARY: - This study aimed to evaluate the efficacy of combined treatment with recombinant interleukin-2 (rIL-2) and allicin on pancreatic cancer and explore the potential immunological mechanism. A total of 60 C57/BL6 nude mice pancreatic cancer xenograft models were randomized into four groups of 15 mice per group: control group, allicin treatment group, rIL-2 treatment group, combined treatment with allicin and rIL-2 group. Mice in each group were treated with saline, rIL-2, allicin, or combination of rIL-2 and allicin by weekly i.v injection for four weeks. After four weeks of treatment, eyeballs of the mice were extracted and blood was drawn, percentages of CD4+T, CD8+T and NK cell were analyzed by FACS, IFN-gamma level was detected by ELISA. One mouse in each group was sacrificed to measure the weight and volume of the tumor and prepared to the paraffin section of tumor tissue. Apoptosis of the tumor cells was analyzed by TUNEL and FACS. Other mice continued to receive treatment, survival period were compared between each group. We observed a significant suppression of xenograft growth and a significant prolonged survival time in the combined treatment with allicin and rIL-2 group ($P < 0.05$). The most amount of apoptotic cells were observed in the combined therapy group ($P < 0.05$). The percentages of CD4+T, CD8+T and NK cell and serum IFN-gamma level increased significantly in the combined treatment group compared with other groups ($P < 0.05$). Combined treatment with allicin and rIL-2 resulted in suppression of tumor growth and prolonged survival time possibly through activation of CD4+T, CD8+T and NK cell.

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[137]
TÍTULO / TITLE: - Prognostic Significance of the Highest Peripancreatic Lymph Node in Biliary Tract Adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Nov 9.
●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3352-4
AUTORES / AUTHORS: - Kelly KJ; Dukleska K; Kuk D; Kingham TP; D'Angelica MI; Dematteo RP; Allen PJ; Jarnagin WR; Fong Y
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.
RESUMEN / SUMMARY: - BACKGROUND: Patients with biliary tract adenocarcinoma with nodal involvement have a poor prognosis. There is currently no standardized method for intraoperative lymph node assessment. The current study aimed to determine the prognostic significance of the highest peripancreatic lymph node (HPLN)

in biliary tract malignancy. METHODS: This was a retrospective study of patients undergoing potential curative resection of biliary tract adenocarcinoma from January 1995 through December 2010 who prospectively had intraoperative sampling of the HPLN. The median follow-up was 72.8 months. The primary end points were recurrence-free survival (RFS) and disease-specific survival (DSS). RESULTS: The rate of HPLN positivity in 110 patients undergoing exploration for potential curative resection was 30 % and did not vary with histologic subtype (gallbladder vs. cholangiocarcinoma). Eighty-five patients underwent complete gross resection. In this subset, median RFS and DSS were 34.3 months (95 % confidence interval [CI] 23.6-not reached [NR]) and 62.4 months (95 % CI 40.8-NR) for HPLN-negative patients, and 9.6 months (95 % CI 4.76-NR) and 20.5 months (95 % CI 7.4-NR) for HPLN-positive patients ($p < 0.01$), respectively. Median DSS was 14.6 months (95 % CI 9.6-25.4) for patients with unresectable disease. On multivariate analysis, HPLN status was an independent predictor of RFS (hazard ratio 3.73, 95 % CI 1.86-7.45; $p < 0.01$) and DSS (hazard ratio 3.98, 95 % CI 1.89-8.38; $p < 0.01$). CONCLUSIONS: HPLN status is prognostic of RFS and DSS in biliary tract adenocarcinoma. Intraoperative nodal staging by HPLN sampling warrants further investigation in a prospective trial.

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[138]

TÍTULO / TITLE: - Use of diffusion-weighted MRI to differentiate chronic pancreatitis from pancreatic cancer.

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

REVISTA / JOURNAL: - AJR Am J Roentgenol. 2013 Nov;201(5):1002-8. doi: 10.2214/AJR.12.10170.

●● Enlace al texto completo (gratuito o de pago) 2214/AJR.12.10170

AUTORES / AUTHORS: - Sandrasegaran K; Nutakki K; Tahir B; Dhanabal A; Tann M; Cote GA

INSTITUCIÓN / INSTITUTION: - 1 Department of Radiology, Indiana University School of Medicine, 550 N University Blvd, UH 0279, Indianapolis, IN, 46202.

RESUMEN / SUMMARY: - OBJECTIVE. The purpose of this study was to compare diffusion-weighted MRI (DWI) and conventional (non-DWI) MRI sequences in differentiating mass-forming chronic pancreatitis from pancreatic cancer. MATERIALS AND METHODS. A retrospective cohort study included 36 patients who underwent pancreatic resection for pancreatic cancer (n = 13) and chronic pancreatitis (n = 23) after preoperative MRI with DWI. Two independent reviewers assessed the DW images for signal intensity and apparent diffusion coefficient (ADC) values. Four weeks later, they reviewed the other MR images for size of mass, double-duct sign, pancreatic duct cutoff, and perivascular soft-tissue cuffing. A score for conventional MRI was given with 1 meaning definitely benign and 5 meaning definitely malignant. Univariate and multivariate analyses and receiver operating characteristic (ROC) curve analysis were performed with surgical pathologic examination as the reference standard. RESULTS. The only finding that differentiated the two groups was the presence of a well-defined mass, favoring the diagnosis of cancer ($p = 0.02$, $p < 0.01$). There was no significant difference between the two groups in signal intensity on DW images ($p = 0.82$, $p = 0.85$) or ADC ($p = 0.51$, $p = 0.76$). Double-duct sign, pancreatic duct cutoff, and perivascular soft-tissue cuffing were not useful in differentiating the two groups. The areas under the ROC curve were 0.873 and 0.878 for the conventional MRI scores,

compared with 0.602 and 0.552 for ADC measurements (p = 0.02, p = 0.008). CONCLUSION. The addition of DWI to conventional MRI does not facilitate differentiation of pancreatic cancer from chronic pancreatitis.

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[139]

TÍTULO / TITLE: - Sporadic nonfunctioning pancreatic neuroendocrine tumors: Prognostic significance of incidental diagnosis.

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

REVISTA / JOURNAL: - Surgery. 2013 Nov 12. pii: S0039-6060(13)00465-0. doi: 10.1016/j.surg.2013.08.007.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.08.007

AUTORES / AUTHORS: - Birnbaum DJ; Gaujoux S; Cherif R; Dokmak S; Fuks D; Couvelard A; Vullierme MP; Ronot M; Ruszniewski P; Belghiti J; Sauvanet A

INSTITUCIÓN / INSTITUTION: - Department of Hepato-Pancreato-Biliary Surgery - Pole des Maladies de l'Appareil Digestif (PMAD), AP-HP, hopital Beaujon, Clichy, France.

RESUMEN / SUMMARY: - BACKGROUND: Sporadic nonfunctioning pancreatic neuroendocrine tumors (NF-PNETs) are increasingly diagnosed as incidentalomas, and their resection is usually recommended. The prognostic significance of this diagnosis feature is poorly studied, and management of these tumors remains controversial. Clinical, pathologic characteristics and outcome of resected incidentally diagnosed NF-PNET (Inc) were compared with resected symptomatic NF-PNET (Symp) to better assess their biologic behavior and tailor their management. METHODS: From 1994 to 2010, 108 patients underwent resection for sporadic nonmetastatic NF-PNET. Diagnosis was considered as incidental in patients with no abdominal symptoms or symptoms unlikely to be related to tumor mass. Patients with Inc were compared with patients with Symp, regarding demographics, postoperative course, pathology, and disease-free survival (DFS). RESULTS: Of the 108 patients, 65 (61%) had incidentally diagnosed tumors. Pancreas-sparing pancreatectomies (enucleation/central pancreatectomy) were performed more frequently in Inc (62% vs 30%, P = .001). Inc tumors were more frequently <20 mm (65% vs 42%, P = .019), staged T1 (62% vs 33%, P = .0001), node negative (85% vs 60%; P = .005), and grade 1 (66% vs 33%, P = .0001). One postoperative death occurred in the Inc group, and postoperative morbidity was similar between the two groups (60% vs 65%, P = .59). DFS was substantially better in the Inc group (5-year DFS = 92% vs 82%, P = .0016). CONCLUSION: Incidentally diagnosed NF-PNETs are associated with less aggressive features compared with symptomatic lesions but cannot always be considered to be benign. Operative resection remains recommended for most. Incidentally diagnosed NF-PNET may be good candidates for pancreas-sparing pancreatectomies.

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[140]

TÍTULO / TITLE: - Prognostic significance of microRNA-141 expression and its tumor suppressor function in human pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Mol Cell Biochem. 2013 Nov 17.

●● Enlace al texto completo (gratuito o de pago) 1007/s11010-013-1897-y

AUTORES / AUTHORS: - Zhu ZM; Xu YF; Su QJ; Du JD; Tan XL; Tu YL; Tan JW; Jiao HB

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, First Hospital Affiliated to the Chinese PLA General Hospital, Fucheng Road 51, Haidian District, Beijing, 100048, China.

RESUMEN / SUMMARY: - Increasing evidence shows that dysregulation of microRNAs is correlated with tumor development. This study was performed to determine the expression of miR-141 and investigate its clinical significance in pancreatic ductal adenocarcinoma (PDAC). Taqman quantitative RT-PCR was used to detect miR-141 expressions in 94 PDAC tissues and 16 nontumorous pancreatic tissues. Correlations between miR-141 expression and clinicopathologic features and prognosis of patients were statistically analyzed. The effects of miR-141 expression on growth and apoptosis of PDAC cell line (PANC-1) were determined by MTT, colony formation, and flow cytometry assays. Potential target genes were identified by luciferase reporter and Western blot assays. The expression level of miR-141 in PDAC tissues was significantly lower than that in corresponding nontumorous tissues. Downregulation of miR-141 correlated with poorer pT and pN status, advanced clinical stage, and lymphatic invasion. Also, low miR-141 expression in PDAC tissues was significantly correlated with shorter overall survival, and multivariate analysis showed that miR-141 was an independent prognostic factor for PDAC patients. Further, functional researches suggested that miR-141 inhibits growth and colony formation, and enhances caspase-3-dependent apoptosis in PANC-1 cells by targeting Yes-associated protein-1 (YAP1). Therefore, miR-141 is an independent prognostic factor for PDAC patients, and functions as a tumor suppressor gene by targeting YAP1.

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[141]

TÍTULO / TITLE: - Evaluation of Ki-67 index in EUS-FNA specimens for the assessment of malignancy risk in pancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - Endoscopy. 2013 Nov 11.

●● Enlace al texto completo (gratuito o de pago) 1055/s-0033-1344958

AUTORES / AUTHORS: - Hasegawa T; Yamao K; Hijioka S; Bhatia V; Mizuno N; Hara K; Imaoka H; Niwa Y; Tajika M; Kondo S; Tanaka T; Shimizu Y; Kinoshita T; Kohsaki T; Nishimori I; Iwasaki S; Saibara T; Hosoda W; Yatabe Y

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Aichi Cancer Center Hospital, Nagoya, Japan.

RESUMEN / SUMMARY: - Background and study aim: Malignancy in pancreatic neuroendocrine tumors (PNETs) is graded by assessing the resected specimens according to the World Health Organization (WHO) 2010 criteria. The feasibility of such grading using endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) specimens remains unclear. The aim of this study was to ascertain the optimal method of measuring the Ki-67 index in EUS-FNA specimens, using resected specimens as the criterion standard. Patients and methods: A total of 58 consecutive patients diagnosed with PNETs between March 1998 and May 2011 were included. The study measured intratumoral Ki-67 index heterogeneity, concordance rates of PNET grading by EUS-FNA with grade of the resected tumor, optimal method of measuring the Ki-67 index in EUS-FNA specimens, and survival analysis based on EUS-FNA specimen grading.

Results: Intratumoral dispersion of Ki-67 index in resected specimens was 0.033 for Grade 1 and 0.782 for Grade 2 tumors (P < 0.001). Concordance rates for WHO classification between EUS-FNA and resected specimens were 74.0 % using the mean Ki-67 index in EUS-FNA specimens and 77.8 % using the highest Ki-67 index. The concordance rate rose to 90 % when EUS-FNA samples with less than 2000 tumor cells were excluded (26 % of EUS-FNA cases). The Kaplan-Meier survival curves were significantly stratified by the EUS-FNA grading of PNETs with 5-year survival rates of 100 %, 58.3 %, and 0 %, for Grade 1, Grade 2, and neuroendocrine carcinoma (NEC) tumors, respectively. Conclusions: Grading of PNETs by the highest Ki-67 index in EUS-FNA specimens with adequate cellularity has a high concordance with grading of resected specimens, and can predict long term patient survival with high accuracy.

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[142]

TÍTULO / TITLE: - Mesopancreas: A boundless structure, namely R1 risk in pancreaticoduodenectomy for pancreatic head carcinoma.

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

REVISTA / JOURNAL: - Eur J Surg Oncol. 2013 Dec;39(12):1303-8. doi: 10.1016/j.ejso.2013.10.012. Epub 2013 Oct 25.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ejso.2013.10.012

AUTORES / AUTHORS: - Peparini N; Chirletti P

INSTITUCIÓN / INSTITUTION: - Azienda Sanitaria Locale Roma H, Distretto H3, via Mario Calo, 5, Ciampino, 00043 Rome, Italy. Electronic address: nadiapeparini@yahoo.it.

RESUMEN / SUMMARY: - BACKGROUND: The mesopancreatic resection margin after pancreaticoduodenectomy for carcinoma of the head of the pancreas is of great interest with respect to curative resection, since the neoplastic involvement of this margin was shown to be the primary site for R1 resection. In this review the current knowledges of the surgical anatomy of the so-called mesopancreas and the mesopancreas excision techniques are summarized. METHODS: References were identified by searching Pubmed database using the search terms “mesopancreas” and “meso-pancreatoduodenum” until June 2013 and through searches of the authors’ own files. Five studies were included in this review. RESULTS: Original contributions with regard to the anatomy of the retropancreatic area and specific technical descriptions of so-called “total mesopancreas excision” provided by published studies are pointed out. CONCLUSIONS: Because there is no “meso” of the pancreas, and due to the continuity of the mesopancreatic and para-aortic areas, surgical dissection should be extended to the left of the superior mesenteric artery and include the para-aortic area to achieve the most complete possible resection of the so-called mesopancreas and minimize the rate of R1 resections due to mesopancreatic margin involvement. This extended mesopancreatic resection cannot be accomplished en bloc even if the removal of the dissected mesopancreatic tissues is performed en bloc with the head, uncus, and neck of the pancreas, i.e., with the pancreaticoduodenectomy specimen.

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[143]

TÍTULO / TITLE: - S-1 plus CIK as second-line treatment for advanced pancreatic cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Med Oncol. 2013 Dec;30(4):747. doi: 10.1007/s12032-013-0747-9. Epub 2013 Oct 13.

●● Enlace al texto completo (gratuito o de pago) 1007/s12032-013-0747-9

AUTORES / AUTHORS: - Wang M; Shi SB; Qi JL; Tang XY; Tian J
INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Shan Dong Ji Ning First People's Hospital, Jining, 272111, People's Republic of China.
RESUMEN / SUMMARY: - This study aimed to evaluate the efficacy and tolerability of S-1 (Tegafur, Gimeracil, and Oteracil Potassium Capsules) plus CIK (Cytokine-induced killer cells) in patients with advanced pancreatic cancer who had previously received gemcitabine-based therapy. In this prospective study, fifty-eight patients were randomly divided into two groups. One group (CT group) was given S-1 alone, and the other group (immuno-CT group) was given S-1 plus CIK. S-1 was administered orally twice a day at 80 mg/m(2)/day on days 1-21 of a 28-day cycle till disease progression or unacceptable toxicity occurred. CIK was given for one cycle of 28 days. The disease control rate for S-1 and CIK was 40.0 and 53.6%, respectively (p = 0.621). The serum CA19-9 level decreased for more than 25% was significantly different (33.3 and 60.7 % in CT group and immuno-CT group, respectively, p = 0.037). The median time to progression was 2.5 (95% CI 2.3-2.8) and 2.9 (95% CI 2.6-3.2) months (p = 0.037) for CT group and immuno-CT group, respectively. The median overall survival was 6.1 (95% CI 5.7-6.5) and 6.6 (95% CI 6.1-7.1) months (p = 0.09) for CT group and immuno-CT group, respectively. The difference in hematological toxicity, including leukocytopenia, anemia, and neutropenia, was insignificant between the two groups. In contrast, the differences in non-hematological toxicity, fatigue, and non-infective fever were significantly different between the two groups (p < 0.05). The S-1 plus CIK regimen was well tolerated in a second-line setting in patients with gemcitabine-refractory and advanced pancreatic cancer.

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[144]
TÍTULO / TITLE: - Histological advantages of the tumor graft: a murine model involving transplantation of human pancreatic cancer tissue fragments.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreas. 2013 Nov;42(8):1275-82. doi: 10.1097/MPA.0b013e318296f866.

●● Enlace al texto completo (gratuito o de pago) 1097/MPA.0b013e318296f866

AUTORES / AUTHORS: - Akashi Y; Oda T; Ohara Y; Miyamoto R; Hashimoto S; Enomoto T; Yamada K; Kobayashi A; Fukunaga K; Ohkochi N
INSTITUCIÓN / INSTITUTION: - From the Department of Surgery, Clinical Sciences, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tsukuba, Ibaraki, Japan.
RESUMEN / SUMMARY: - OBJECTIVES: Experimental data based on cell line-derived xenograft models (cell xenograft) seldom reproduce the clinical situation, and therefore we demonstrated here the superiority of a murine model involving transplantation of human pancreatic cancer tissue fragments (tumor graft), focusing on the histological features and drug delivery characteristics. METHODS: Tumor pieces from 10 pancreatic cancer patients were transplanted into SCID (severe combined

immunodeficient) mice. Histological characteristics of tumor grafts, including morphology, desmoplastic reaction, and vascularization, were compared with those of cell xenografts. Drug delivery was evaluated by quantifying the concentrations of injected drug, and the results were compared with its histological features. RESULTS: Eight of the 10 transplanted tumors successfully engrafted. Histological comparisons between tumor grafts and cell xenografts revealed the following: the amount of stroma was more (22.9% +/- 11.8% vs 10.8% +/- 5.4%; P < 0.05), vessel-cancer cell distance was longer (35.3 +/- 39.0 vs 3.9 +/- 3.1 mum; P < 0.001), and microvessel density was lower (6.8 +/- 1.9 vs 10.8 +/- 2.1 vessels/0.4 mm; P < 0.05) in tumor grafts. Drug concentrations in tumor grafts were lower than those in cell xenografts (3.3 +/- 1.2 vs 6.0+/-0.2 mug/mL; P = 0.003), and the differences were correlated with the histological differences. CONCLUSIONS: Pancreatic tumor grafts better reproduce the histological nature of clinical cancer and thus provide a more realistic model that is applicable for pharmacokinetic studies.

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[145]

TÍTULO / TITLE: - Effects of integrin-targeted photodynamic therapy on pancreatic carcinoma cell.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Oct 21;19(39):6559-67. doi: 10.3748/wjg.v19.i39.6559.

●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i39.6559

AUTORES / AUTHORS: - Zhou M; Ni QW; Yang SY; Qu CY; Zhao PC; Zhang JC; Xu LM

INSTITUCIÓN / INSTITUTION: - Min Zhou, Qian-Wen Ni, Shan-Ying Yang, Chun-Ying Qu, Lei-Ming Xu, Digestive Endoscopic Diagnosis and Treatment Center, Xinhua Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai 200092, China.

RESUMEN / SUMMARY: - AIM: To investigate the effects of photodynamic therapy with quantum dots-arginine-glycine-aspartic acid (RGD) probe as photosensitizer on the proliferation and apoptosis of pancreatic carcinoma cells. METHODS: Construction of quantum dots-RGD probe as photosensitizer for integrin-targeted photodynamic therapy was accomplished. After cells were treated with photodynamic therapy (PDT), the proliferation of SW1990 cells were measured by methyl thiazolyl tetrazolium assay. Morphologic changes, cell cycle retardance and apoptosis were observed under fluoroscope and flow cytometry. The expression of myeloid cell leukemia-1 (Mcl-1), protein kinase B (Akt) and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) mRNA were detected by reverse transcription-polymerase chain reaction. The amount of reactive oxygen species were also evaluated by fluorescence probe. RESULTS: The photodynamic therapy with quantum dots-RGD probe as photosensitizer significantly inhibited cell proliferation (P < 0.01). Apoptotic cells and morphologic changes could be found under optical microscope. The FCM revealed PDT group had more significant cell apoptosis rate compared to control cells (F = 130.617, P < 0.01) and cell cycle G0/G1 and S retardance (P < 0.05) compared to control cells. The expression of Mcl-1 and Akt mRNA were down-regulated, while expression of TRAIL mRNA was up-regulated after cells treated with PDT. PDT group had more significant number of cells producing reactive oxygen species compared to control cells (F = 3262.559, P < 0.01). CONCLUSION: The photodynamic therapy with

quantum dots-RGD probe as photosensitizer significantly inhibits cell proliferation and increases apoptosis in SW1990 cells.

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[146]
TÍTULO / TITLE: - Differential diagnosis of benign and malignant distal biliary strictures: Value of adding diffusion-weighted imaging to conventional magnetic resonance cholangiopancreatography.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Magn Reson Imaging. 2013 Oct 17. doi: 10.1002/jmri.24304.
●● Enlace al texto completo (gratuito o de pago) 1002/jmri.24304
AUTORES / AUTHORS: - Yoo RE; Lee JM; Yoon JH; Kim JH; Han JK; Choi BI
INSTITUCIÓN / INSTITUTION: - Department of Radiology, Seoul National University College of Medicine, Seoul, Korea.
RESUMEN / SUMMARY: - PURPOSE: To determine the value of adding diffusion-weighted imaging (DWI) to conventional magnetic resonance cholangiopancreatography (MRCP) for differentiating benign from malignant distal biliary strictures. MATERIALS AND METHODS: Two independent readers reviewed three image sets (1: MRCP alone; 2: MRCP and DWI combined; and 3: MRCP, DWI, and contrast-enhanced T1-weighted imaging [T1WI] combined) of 60 patients with suspected distal biliary strictures and rated the probability of malignancy. Diagnostic performance and accuracy were compared using the receiver operating characteristic (ROC) curves and McNemar two-tailed test. kappa coefficients were calculated to assess the interobserver agreement. RESULTS: The Az value and accuracy improved significantly after additional review of DWI for both readers: Az = 0.780 vs. 0.916 (P = 0.003) for Reader 1 and 0.784 vs. 0.853 (P = 0.037) for Reader 2; accuracy = 69% vs. 93% for Reader 1 (P < 0.001) and 57% vs. 85% for Reader 2 (P = 0.002). No significant difference in the Az values and accuracy was found between MRCP and DWI combined, and MRCP, DWI, and contrast-enhanced T1WI combined (P > 0.050). There was substantial interobserver agreement in all three image sets (kappa = 0.695-0.732). CONCLUSION: The addition of DWI to MRCP significantly improved diagnostic accuracy in the characterization of distal biliary strictures. J. Magn. Reson. Imaging 2013. © 2013 Wiley Periodicals, Inc.

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[147]
TÍTULO / TITLE: - A prospective, claims-based assessment of the risk of pancreatitis and pancreatic cancer with liraglutide compared to other antidiabetic drugs.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Diabetes Obes Metab. 2013 Nov 6. doi: 10.1111/dom.12230.
●● Enlace al texto completo (gratuito o de pago) 1111/dom.12230
AUTORES / AUTHORS: - Funch D; Gydesen H; Tornoe K; Major-Pedersen A; Chan KA
INSTITUCIÓN / INSTITUTION: - Optum, Epidemiology, Waltham, MA, USA.
RESUMEN / SUMMARY: - AIM: We evaluated the relationship between liraglutide and acute pancreatitis or pancreatic cancer in an ongoing post-marketing safety assessment programme. METHODS: Initiators of liraglutide, exenatide, metformin, pioglitazone or groups containing initiators of dipeptidyl peptidase-4 inhibitors or sulfonylureas were identified in a US commercial health insurance claims database (1

February 2010 to 31 March 2013) and followed for a median of 15 months. We estimated incidence rates (IR/100 000 person-years), rate ratio (RR) and 95% confidence intervals (CI) of new insurance claims with diagnoses of primary inpatient acute pancreatitis or pancreatic cancer from Poisson regression models. RESULTS: The IR for acute pancreatitis for liraglutide was 187.5 compared with 154.4 for all non-glucagon-like peptide-1 (GLP-1)-based therapies (adjusted RR 1.10; CI 0.81-1.49). The IR for pancreatic cancer was 19.9 for liraglutide compared with 33.0 for all non-GLP-1-based therapies (adjusted RR 0.65; 95% CI 0.26-1.60). CONCLUSION: We did not observe excess risk of either outcome associated with liraglutide relative to individual or pooled comparator drugs.

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[148]

TÍTULO / TITLE: - Solid pseudopapillary neoplasm of the pancreas in children: a 15-year experience and the identification of a unique immunohistochemical marker.

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

REVISTA / JOURNAL: - J Pediatr Surg. 2013 Oct;48(10):2054-60. doi: 10.1016/j.jpedsurg.2013.02.068.

●● Enlace al texto completo (gratuito o de pago) 1016/j.jpedsurg.2013.02.068

AUTORES / AUTHORS: - Laje P; Bhatti TR; Adzick NS

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Children's Hospital of Philadelphia, Philadelphia, PA, USA.

RESUMEN / SUMMARY: - PURPOSE: To review our 15-year experience in the management of children with solid pseudopapillary neoplasm (SPPN) of the pancreas at a single pediatric institution, to delineate a unique immunohistochemical marker for SPPN, and to analyze cumulative data on this rare entity in the literature. METHODS: We did a retrospective analysis of the demographic data, clinical presentation, immunohistochemical characteristics, surgical approach, and long-term outcomes of all patients diagnosed with SPPN between 1997 and 2012. RESULTS: There were 6 patients in the series, 5 females and 1 male. Median age at presentation and at surgery was 15 years (11-18 years). Abdominal pain was the presenting symptom in 5 cases and jaundice in 1 case. Two patients had a pancreatic head tumor and underwent a pylorus-preserving pancreaticoduodenectomy. Two patients had the tumor in the pancreatic tail and underwent a distal pancreatectomy with splenectomy. Two patients had the tumor in the pancreatic body and underwent a distal pancreatectomy with splenectomy in one case and with preservation of the spleen in the other. All tumors were completely resected with pathologic margins free of disease. The median maximum diameter was 6.8 cm (3 to 15 cm). On immunohistochemistry the tumors exhibited different combinations of non-specific markers like chromogranin, vimentin and neuron-specific enolase, but all tumors showed the highly SPPN-specific paranuclear dot-like immunoreactivity pattern for CD99 in the solid as well as in the pseudopapillary areas. No patient had metastasis at presentation. Median follow-up was 6.5 years (6 months to 15 years). There were no recurrences, no long-term metastasis, and all patients are disease-free. CONCLUSION: Our series supports the concept that complete resection is necessary to achieve the best possible long-term results. Additionally, we demonstrate that SPPN exhibits a very unique immunostaining pattern for CD99 that is present in all cases.

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[149]

TÍTULO / TITLE: - Phosphorylation of STAT3 correlates with HER2 status, but not with survival in pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - APMIS. 2013 Oct 29. doi: 10.1111/apm.12194.

●● Enlace al texto completo (gratuito o de pago) 1111/apm.12194

AUTORES / AUTHORS: - Koperek O; Aumayr K; Schindl M; Werba G; Soleiman A; Schoppmann S; Sahora K; Birner P

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Medical University of Vienna, Vienna.

RESUMEN / SUMMARY: - Activation of signal-transcriptional factor signal transducer and activator of transcription 3 (STAT3) is associated with more aggressive behaviour in a variety of human malignancies. As selective STAT3 inhibitors exist, this protein might represent a novel therapeutic target. Although STAT3 seems to play an important role in progression of pancreatic ductal carcinoma (PDAC), only few data on this subject exist. The aim of our study was the investigation of STAT3 activation and its correlation with its possible regulator HER2. Expression of tyrosine-705 phosphorylated STAT3 (pSTAT3) was determined immunohistochemically in 79 PDACs. HER2 status assessed by immunohistochemistry and double colour silver in situ hybridization was available from a previous study. PSTAT3 expression was seen in 33 (41.8%) patients. Six patients were scored as HER2 positive having strong correlation with pSTAT3 expression (p = 0.004, Fisher's exact test). No association of pSTAT3 expression with patients' age, tumour staging and grading, perineural invasion of tumour cells or survival time was seen. pSTAT3 is frequently expressed in PDAC. Nevertheless, its immediate clinical relevance seems to be low. However, further research needs to determine whether STAT3 status in PDAC is predictive for the response to novel targeting therapies.

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[150]

TÍTULO / TITLE: - Expression of major histocompatibility complex class I-related chain A/B (MICA/B) in pancreatic carcinoma.

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

REVISTA / JOURNAL: - Int J Oncol. 2014 Jan;44(1):99-104. doi: 10.3892/ijo.2013.2156. Epub 2013 Oct 31.

●● Enlace al texto completo (gratuito o de pago) 3892/ijo.2013.2156

AUTORES / AUTHORS: - Dambrauskas Z; Svensson H; Joshi M; Hyltander A; Naredi P; Iresjo BM

INSTITUCIÓN / INSTITUTION: - Department of Surgery and Institute for Research of Digestive System, Lithuanian University of Health Sciences, Kaunas, Lithuania.

RESUMEN / SUMMARY: - Major histocompatibility complex class I-related chain A and B (MICA/B) are two stress-inducible ligands that bind to the immunoreceptor NKG2D and play an important role in mediating cytotoxicity of NK and T cells. Release of MIC molecules from the cell surface is thought to constitute an immune escape mechanism of tumor cells and thus could be associated with more aggressive course of tumor growth. In this study, we investigated the expression of MICA/B in ductal pancreatic carcinoma and serum in relation to tumor stage, differentiation and survival. MICA/B

expression in tumor tissues and sera from patients with pancreatic cancer were analyzed by immunohistochemical staining (IHC), western blotting and ELISA, respectively. MICA/B expression was present in 17 of 22 (77%) of the tumors but not in normal pancreatic ductal epithelial cells. Poorly differentiated tumors showed more pronounced MICA/B expression compared to differentiated tumors, but did not correlate significantly to other tumor characteristics. MICA/B-negative tumors displayed significantly lower incidence of lymph node metastases ($p<0.01$), and less mortality within 3 years following resection ($p<0.02$). In conclusion, tissue levels of MICA/B expression were elevated in pancreatic cancer cells without elevated levels in serum, despite well-recognized acute phase reactants in serum. Poorly differentiated tumors showed high MICA/B expression, which was related to extended tumor lymph node metastases and less frequent long-term survival.

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[151]

TÍTULO / TITLE: - Intensity of Follow-up after Pancreatic Cancer Resection.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Oct 4.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3289-7

AUTORES / AUTHORS: - Castellanos JA; Merchant NB

INSTITUCIÓN / INSTITUTION: - Division of Surgical Oncology and Endocrine Surgery, Vanderbilt University Medical Center, Nashville, TN, USA.

RESUMEN / SUMMARY: - The prognosis of patients diagnosed with pancreatic adenocarcinoma remains dismal. Of the 15-20 % of patients who are candidates for potentially curative resection, 66-92 % will develop recurrent disease. Although guidelines for surveillance in the postoperative setting exist, they are not evidence based, and there is wide variability of strategies utilized. Current surveillance guidelines as suggested by the National Comprehensive Cancer Network (NCCN) include routine history and physical, measurement of serum cancer-associated antigen 19-9 (CA19-9) levels, and computed tomographic imaging at 3- to 6-month intervals for the first 2 years, and annually thereafter. However, the lack of prospective clinical data examining the efficacy of different surveillance strategies has led to a variability of the intensity of follow-up and a lack of consensus on its necessity and efficacy. Recent therapeutic advances may have the potential to significantly alter survival after recurrence, but a careful consideration of current surveillance strategies should be undertaken to optimize existing approaches in the face of high recurrence and low survival rates.

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[152]

TÍTULO / TITLE: - EZH2-shRNA-mediated upregulation of p21waf1/cip1 and its transcriptional enhancers with concomitant downmodulation of mutant p53 in pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Surgery. 2013 Oct;154(4):739-46; discussion 746-7. doi: 10.1016/j.surg.2013.06.041.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.06.041

AUTORES / AUTHORS: - Batchu RB; Qazi AM; Gruzdyn OV; Semaan A; Seward SM; Chamala S; Dhulipala VB; Bouwman DL; Weaver DW; Gruber SA

INSTITUCIÓN / INSTITUTION: - Laboratory of Surgical Oncology & Developmental Therapeutics, Department of Surgery, Wayne State University, Detroit, MI; John D. Dingell VA Medical Center, Wayne State University, Detroit, MI. Electronic address: rbatchu@med.wayne.edu.

RESUMEN / SUMMARY: - PURPOSE: Enhancer of zeste homologue 2 (EZH2), a component of the chromatin modification protein complex, is upregulated in pancreatic ductal adenocarcinoma (PDAC), whereas loss of p53 and its downstream target, p21(waf1/cip1), is also observed frequently. We sought to investigate the role of the p53-p21(waf1/cip1) pathway in relation to EZH2-mediated inhibition of PDAC. METHODS: The PANC-1 cell line was utilized in chromatin immunoprecipitation, gene profiling, Western blot, cell invasion, cell proliferation, and tumor xenograft assays. RESULTS: Western blot analysis with antibodies that recognize both wild-type and mutant p53 did not show any alterations in band intensity; however, antibody that detects only mutant p53 showed a band of significantly lesser intensity with EZH2 knockdown. Western blot analysis further revealed a significant upregulation of p21(waf1/cip1). Gene expression profile analysis indicated significantly enhanced transcripts of transcriptional inducers of p21(waf1/cip1), with downregulation of mutant p53 transcript, corroborating the Western blot analysis. PANC-1 cells expressing EZH2-short hairpin RNA displayed markedly attenuated growth in SCID mice. CONCLUSION: Downregulation of mutant p53 with concomitant enhanced expression of p21(waf1/cip1) and its transcriptional trans-activators may contribute toward EZH2-mediated suppression of PDAC.

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[153]

TÍTULO / TITLE: - Sineoculis homeobox homolog 1 protein overexpression as an independent biomarker for pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Exp Mol Pathol. 2013 Nov 18. pii: S0014-4800(13)00137-8. doi: 10.1016/j.yexmp.2013.11.003.

●● Enlace al texto completo (gratuito o de pago) 1016/j.yexmp.2013.11.003

AUTORES / AUTHORS: - Jin A; Xu Y; Liu S; Jin T; Li Z; Jin H; Lin L; Lin Z

INSTITUCIÓN / INSTITUTION: - Key Laboratory of Changbai Mountain Biological Resources and Functional Molecule, Ministry of Education, Yanbian University, Yanji 133002, China; Department of Internal Medicine, Yanbian University Hospital, Yanji 133000, China. Electronic address: drjinah@163.com.

RESUMEN / SUMMARY: - Sineoculis homeobox homolog 1 (SIX1) is a member of the SIX gene family. It is highly expressed in cancers derived from tissues that play a fundamental role during embryogenesis. Recent studies suggest that inappropriate expression of SIX1 can both initiate tumorigenesis and promote metastasis. To investigate the clinicopathological significance of SIX1 expression in pancreatic ductal adenocarcinoma (PDAC), and to further identify its role as a potential biomarker and therapeutic target in PDAC, 103 PDAC tissue samples and 45 normal pancreatic tissue samples were immunohistochemically stained for SIX1 protein. The localization of SIX1 protein was detected in Panc-1 cancer cells using immunofluorescence staining. Correlations between SIX1 overexpression and the clinicopathological features of pancreatic cancer were evaluated using Chi-square (chi2) tests, differences in survival curves were analyzed using log-rank tests, and multivariate survival

analysis was performed using the Cox proportional hazard regression model. In results, SIX1 protein showed mainly cytoplasmic/perinuclear staining pattern in PDAC with immunohistochemistry. The strongly positive rate of SIX1 protein was 60.2% (62/103) in PDAC, which was significantly higher than normal pancreatic tissue (6.7%, 3/45). SIX1 overexpression was positively correlated with tumor size, TNM stage, lymph node metastasis, and grade of PDAC (P<0.001). SIX1 high expression levels influenced overall survival rates in G1, G2, stage I-II and stage III-IV groups of PDAC; and high expression levels had significantly lower overall survival rates than SIX1 low expression levels. In conclusion, SIX1 emerged as a significant independent prognostic factor in PDAC. SIX1 overexpression appears to be associated with PDAC, and may be a potential biomarker for early diagnosis and prognostic evaluation of PDAC.

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[154]

TÍTULO / TITLE: - Cholecystokinin (CCK) and Pancreatic Cancer: the Chicken or the Egg?

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

REVISTA / JOURNAL: - Am J Physiol Gastrointest Liver Physiol. 2013 Oct 31.

●● Enlace al texto completo (gratuito o de pago) 1152/ajpgi.00301.2013

AUTORES / AUTHORS: - Smith JP; Solomon TE

INSTITUCIÓN / INSTITUTION: - 1National Institutes of Health.

RESUMEN / SUMMARY: - The gastrointestinal peptide cholecystokinin (CCK) causes the release of pancreatic digestive enzymes and growth of the normal pancreas. Exogenous CCK administration has been used in animal models to study pancreatitis and also as a promoter of carcinogen-induced or Kras-driven pancreatic cancer. Defining CCK receptors in normal human pancreas has been problematic due to its retroperitoneal location, high concentrations of pancreatic proteases, and endogenous RNase. Most studies indicate that the predominant receptor in human pancreas is the CCK-B type, and CCK-A is the predominant form in rodent pancreas. In pancreatic cancer cells and tumors, the role of CCK is better established because receptors are often over-expressed by these cancer cells and stimulation of such receptors promotes growth. Furthermore, in established cancer, endogenous production of CCK and/or gastrin occurs and their actions stimulate the synthesis of more receptors plus growth by an autocrine mechanism. Initially it was thought that the mechanism by which CCK served to potentiate carcinogenesis was by interplay with inflammation in the pancreatic microenvironment. But with the recent findings of CCK receptors on early PanIN lesions and on stellate cells, the question has been raised that perhaps CCK actions are not the result of cancer but an early driving promoter of cancer. This review will summarize what is known regarding CCK, its receptors, and pancreatic cancer, and also what is unknown and requires further investigation to determine which comes first, the chicken or the egg; ‘CCK or the cancer.”

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[155]

TÍTULO / TITLE: - A retrospective analysis of early CA19-9 change in salvage chemotherapy for refractory pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Oct 12.

●● Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2313-8

AUTORES / AUTHORS: - Nakai Y; Isayama H; Sasaki T; Takahara N; Hamada T; Uchino R; Mizuno S; Miyabayashi K; Yamamoto K; Mohri D; Kogure H; Yamamoto N; Hirano K; Ijichi H; Tateishi K; Tada M; Koike K

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo Bunkyo-ku, Tokyo, 113-8655, Japan.

RESUMEN / SUMMARY: - PURPOSE: In salvage chemotherapy for refractory pancreatic cancer, early assessment is important to avoid unnecessary toxicities from ineffective chemotherapy. Early CA19-9 change after the first course as a prognostic factor was evaluated in this setting. METHODS: Patients receiving salvage chemotherapy were retrospectively studied. CA19-9 was measured prior to and after the first course. Cox regression analysis was performed for prognostic factors for progression-free survival (PFS) and overall survival (OS), using the landmark method defined as a day of CA19-9 measurement after the first course. RESULTS: A total of 239 salvage regimens were given in 167 patients. Median PFS and OS were 2.7 and 6.1 months, respectively. Median pretreatment CA19-9 was 2,362 U/mL, and median CA19-9 change after the first course was 17.8 % increase. CA19-9 change was associated with tumor response, and PFS was 1.7 versus 3.5 months and OS was 3.9 and 8.6 months in patients with >/=50 % versus <50 % increase. In the multivariate analyses, CA19-9 increase >/=50 % was prognostic of both PFS and OS (HR 2.28 and 2.50, p < 0.001, respectively). CONCLUSION: CA19-9 change after the first course was prognostic of PFS and OS in refractory pancreatic cancer. Early discontinuation should be considered given the palliative setting.

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[156]

TÍTULO / TITLE: - Epithelial-to-mesenchymal transition predicts prognosis of pancreatic cancer.

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

REVISTA / JOURNAL: - Surgery. 2013 Nov;154(5):946-54. doi: 10.1016/j.surg.2013.05.004. Epub 2013 Sep 26.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.05.004

AUTORES / AUTHORS: - Yamada S; Fuchs BC; Fujii T; Shimoyama Y; Sugimoto H; Nomoto S; Takeda S; Tanabe KK; Kodera Y; Nakao A

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery (Surgery II), Nagoya University Graduate School of Medicine, Nagoya, Japan. Electronic address: suguru@med.nagoya-u.ac.jp.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer has a dismal prognosis that is attributed to common local invasiveness and metastasis. Epithelial-to-mesenchymal transition (EMT) plays an important role in cancer invasion and metastasis and is associated with early dissemination. The aim of this study was to evaluate the association between EMT and the prognoses for patients with pancreatic cancer. METHODS: Immunohistochemistry of E-cadherin and vimentin was performed on surgical specimens from 174 patients who underwent resection of their pancreatic cancers. Tumoral stainings of E-cadherin and vimentin were graded, and EMT statuses were determined by calculating the ratio of vimentin to E-cadherin, whereby patients were categorized into 3 groups: epithelial, intermediate, and mesenchymal. The correlations between EMT statuses and clinicopathologic factors and prognoses

were analyzed. RESULTS: There was a significant correlation between EMT status and CA19-9 levels (P = .020); peritoneal washing cytology (P = .025); portal vein invasion (P = .038); and lymph node metastasis (P = .030). The median survival for patients with epithelial tumors was 40.2 months as compared to 13.7 months for patients with mesenchymal tumors. Multivariate analysis demonstrated that perineural invasion (P = .024); lymph node metastasis (P = .033); and EMT status (P < .0001) were significant prognostic factors. It is interesting that adjuvant chemotherapy (gemcitabine and/or S-1) improved the median survival time from 10.8 to 16.1 months in patients with mesenchymal tumors (P = .002); however, no significant difference was seen in patients with epithelial tumors. CONCLUSION: EMT status is an important prognostic factor for pancreatic cancer and is associated with portal vein invasion and lymph node metastasis.

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[157]

TÍTULO / TITLE: - Biochanin A reduces pancreatic cancer survival and progression.

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

REVISTA / JOURNAL: - Anticancer Drugs. 2013 Nov 6.

●● Enlace al texto completo (gratuito o de pago)

1097/CAD.0000000000000044

AUTORES / AUTHORS: - Bhardwaj V; Tadinada SM; Jain A; Sehdev V; Daniels CK; Lai JC; Bhushan A

INSTITUCIÓN / INSTITUTION: - aDepartment of Surgery, Vanderbilt University Medical Center, Nashville, Tennessee bDepartment of Biological Sciences, University of Iowa, Iowa City, Iowa cDepartment of Molecular and Biomedical Pharmacology, University of Kentucky, Lexington, Kentucky dDepartment of Pharmaceutical Sciences, Long Island University, Brookville, New York eDepartment of Biomedical and Pharmaceutical Sciences, College of Pharmacy, Idaho State University, Pocatello, Idaho fDepartment of Pharmaceutical Sciences, Jefferson School of Pharmacy, Thomas Jefferson University, Philadelphia, Pennsylvania, USA.

RESUMEN / SUMMARY: - Pancreatic cancer has dismally low mean survival rates worldwide. Only a few chemotherapeutic agents including gemcitabine have been shown to improve the survival of pancreatic cancer patients. Biochanin A, an isoflavone, is known to exert an anticancer effect on various cancer types. In this study, we examined the anticancer properties of biochanin A on pancreatic cancer cells. The effect of biochanin A on cellular survival, apoptosis, and proliferation was analyzed using MTT, flow cytometry, and colony formation assay. The effect of biochanin A on pancreatic cancer's mitogenic signaling was determined using western blot analysis. Migration assay and zymography were used to determine biochanin A's effect on pancreatic cancer progression. Biochanin A induced dose-dependent toxicity on pancreatic cancer cells (Panc1 and AsPC-1). It reduced colony formation ability of Panc1 cells and induced dose-dependent apoptosis. Activation of Akt and MAPK was inhibited. Furthermore, the migratory and invasive potential of the cancer cells was also reduced. The results suggest that biochanin A is effective in reducing pancreatic cancer cell survival by inhibiting their proliferation and inducing apoptosis. It affects mitogenic, migratory, and invasive processes involved in cancer progression. These findings may lead to novel approaches to treat pancreatic cancer using isoflavones in combination with other therapeutic drugs.

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[158]

TÍTULO / TITLE: - New stable isotope method to measure protein digestibility and response to pancreatic enzyme intake in cystic fibrosis.

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

REVISTA / JOURNAL: - Clin Nutr. 2013 Nov 9. pii: S0261-5614(13)00305-1. doi: 10.1016/j.clnu.2013.11.004.

●● Enlace al texto completo (gratuito o de pago) 1016/j.clnu.2013.11.004

AUTORES / AUTHORS: - Engelen MP; Com G; Anderson PJ; Deutz NE

INSTITUCIÓN / INSTITUTION: - Center for Translational Research in Aging & Longevity, Dept. Health and Kinesiology, Texas A&M University, College Station, TX, USA; Center for Translational Research in Aging & Longevity, Dept. Geriatrics, University of Arkansas for Medical Sciences, Little Rock, AR, USA. Electronic address: mpkj.engelen@ctral.org.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Adequate protein intake and digestion are necessary to prevent muscle wasting in cystic fibrosis (CF). Accurate and easy-to-use methodology to quantify protein maldigestion is lacking in CF. OBJECTIVE: To measure protein digestibility and the response to pancreatic enzyme intake in CF by using a new stable isotope methodology. DESIGN: In 19 CF and 8 healthy subjects, protein digestibility was quantified during continuous (sip) feeding for 6 h by adding 15N-labeled spirulina protein and L-[ring-2H5]phenylalanine (PHE) to the nutrition and measuring plasma ratio [15N]PHE to [2H5]PHE. Pancreatic enzymes were ingested after 2 h in CF and the response in protein digestibility was assessed. To exclude difference in mucosal function, postabsorptive whole-body citrulline (CIT) production rate was measured by L-[5-13C-5,5-2H2]-CIT pulse and blood samples were taken to analyze tracer-tracee ratios. RESULTS: Protein digestibility was severely reduced in the CF group (47% of healthy subjects; $P < 0.001$). Intake of pancreatic enzymes induced a slow increase in protein digestibility in CF until 90% of values obtained by healthy subjects. Maximal digestibility was reached at 100 min and maintained for 80 min. Stratification into CF children (n = 10) and adults showed comparable values for protein digestibility and similar kinetic responses to pancreatic enzyme intake. Whole-body citrulline production was elevated in CF indicating preserved mucosal function. CONCLUSION: Protein digestibility is severely compromised in patients with CF as measured by this novel and easy-to-use stable isotope approach. Pancreatic enzymes are able to normalize protein digestibility in CF, albeit with a severe delay. Registration ClinicalTrials.gov = NCT01494909.

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[159]

TÍTULO / TITLE: - Diagnostic Performance of MDCT for Predicting Important Prognostic Factors in Pancreatic Cancer.

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

REVISTA / JOURNAL: - Pancreas. 2013 Nov;42(8):1316-22. doi: 10.1097/MPA.0b013e318287c604.

●● Enlace al texto completo (gratuito o de pago) 1097/MPA.0b013e318287c604

AUTORES / AUTHORS: - Kim JH; Eun HW; Kim KW; Lee JY; Lee JM; Han JK; Choi BI

INSTITUCIÓN / INSTITUTION: - From the *Department of Radiology and Institute of Radiation Medicine, Seoul National University College of Medicine; and daggerHealth Promotion Center, Asan Medical Center, University of Ulsan, Songpa-gu, Seoul, Korea.

RESUMEN / SUMMARY: - OBJECTIVES: Tumor stage, node metastasis, tumor size, vascular invasion, and perineural invasion are the most important prognostic factors that might be determined by preoperative multidetector computed tomography (MDCT) in pancreatic cancer. The purpose of our study is to investigate diagnostic accuracy of MDCT for determining these prognostic factors. METHODS: For 6 years, 111 patients with surgically resected pancreatic cancer underwent preoperative MDCT. Two radiologists retrospectively assessed tumor stage, node metastasis, tumor size, and vascular invasion. They also graded perineural invasion using a 3-point scale focused on 5 routes. Statistical analyses were performed using the receiver operating characteristic analysis, McNemar test, and paired t test. RESULTS: Statistically, tumor size on specimens (3.4 +/- 1.46 cm) is larger than tumor size on MDCT (3.2 +/- 1.41 cm; P = 0.001). The diagnostic accuracy rates for tumor stage were 82.9% and 77.5%, with moderate agreement (kappa = 0.732). The accuracy rates for node metastasis were 59.5% and 55.0%, with fair agreement (kappa = 0.597). The diagnostic accuracy rates for vascular invasion were 94% and 92%. The areas under the curve for perineural invasion were 0.733 and 0.66 (P = 0.069), with moderate agreement (kappa = 0.77). CONCLUSIONS: Multidetector computed tomography is very useful for the preoperative evaluation of tumor stage, perineural invasion, and vascular invasion of pancreatic cancer, but it has limited evaluation of node metastasis and tumor size.

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[160]

TÍTULO / TITLE: - Rate of growth of pancreatic serous cystadenoma as an indication for resection.

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

REVISTA / JOURNAL: - Surgery. 2013 Oct;154(4):794-800; discussion 800-2. doi: 10.1016/j.surg.2013.07.005.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.07.005

AUTORES / AUTHORS: - El-Hayek KM; Brown N; O'Rourke C; Falk G; Morris-Stiff G; Walsh RM

INSTITUCIÓN / INSTITUTION: - Digestive Disease Institute, Cleveland Clinic, Cleveland, OH.

RESUMEN / SUMMARY: - BACKGROUND: The purpose of this study was to examine the natural history and growth rate of pancreatic serous cystadenomas (SCAs) to determine which factors lead to resection for these benign neoplasms. METHODS: We reviewed retrospectively a prospectively maintained database, identifying patients diagnosed with SCAs of the pancreas. The diagnosis was made via a combination of classic imaging features with or without cyst aspiration results consistent with SCA. To determine growth rates, gamma regression models were used and the average was modeled using the log function. RESULTS: A prospectively maintained database of 1,241 pancreatic cystic neoplasms was queried from 1998 to 2010. A total of 219 patients (18%) were diagnosed with SCA, 194 in the surveillance group and 25 in the resection group. Twenty patients underwent resection after initial imaging principally for presence of symptoms and indeterminate diagnosis, and 5 underwent resection after

surveillance for development of symptoms and/or rapid rate of growth. Rate of growth increased at a steady state over time, with an estimated doubling time of 12 years (95% confidence interval, 7.8-21.5). CONCLUSION: This study shows that growth patterns are similar for SCAs of the pancreas regardless of initial size. When doubling time is faster than 12 years, resection should be considered.

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[161]
TÍTULO / TITLE: - miR-15a inhibits cell proliferation and epithelial to mesenchymal transition in pancreatic ductal adenocarcinoma by down-regulating Bmi-1 expression.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cancer Lett. 2013 Nov 16. pii: S0304-3835(13)00738-6. doi: 10.1016/j.canlet.2013.10.009.
●● Enlace al texto completo (gratuito o de pago) 1016/j.canlet.2013.10.009
AUTORES / AUTHORS: - Guo S; Xu X; Tang Y; Zhang C; Li J; Ouyang Y; Ju J; Bie P; Wang H
INSTITUCIÓN / INSTITUTION: - Institute of Hepatopancreatobiliary Surgery, Southwest Hospital, Third Military Medical University, Chongqing 400038, PR China.
RESUMEN / SUMMARY: - PURPOSES: To investigate whether miR-15a inhibits cell proliferation and epithelial-mesenchymal transition (EMT) in pancreatic ductal adenocarcinoma (PDAC) via the down-regulation of B cell-specific moloney murine leukemia virus insertion site 1 (Bmi-1) expression. METHODS AND RESULTS: miR-15a and Bmi-1 expressions in normal pancreatic tissue and PDAC tissue were measured. The relationship between miR-15a and Bmi-1 expression was analyzed. We found that miR-15a suppressed the expression of Bmi-1 and PDAC cell proliferation; E-cadherin expression was visibly up-regulated after silencing Bmi-1 by transfecting miR-15a into PDAC cell line. CONCLUSION: miR-15a inhibits cell proliferation and EMT in PDAC via the down-regulation of Bmi-1 expression.

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[162]
TÍTULO / TITLE: - Evaluation of the effect of comorbidity on survival in pancreatic cancer by using “Charlson Comorbidity Index” and “Cumulative Illness Rating Scale”
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Wien Klin Wochenschr. 2013 Nov 19.
●● Enlace al texto completo (gratuito o de pago) 1007/s00508-013-0453-9
AUTORES / AUTHORS: - Kos FT; Yazici O; Civelek B; Seker M; Arik Z; Aksoy S; Uncu D; Ozdemir N; Zengin N
INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Kahramanmaras Sutcu Imam University Faculty of Medicine, 46000, Merkez, Kahramanmaras, Turkey, tugbasan@yahoo.com.
RESUMEN / SUMMARY: - BACKGROUND: Effect of comorbidity on the treatments that patients receive is not clear, as healthy elderly patients and the elderly with less comorbid diseases are included in the studies. In the present study, the effect of comorbidity on the survival was evaluated using Charlson Comorbidity Index (CCI) and Cumulative Illness Rating Scale (CIRS). MATERIAL AND METHOD: The general features and comorbid diseases of the pancreatic cancer patients were retrospectively screened from the patient files using the automated system. CCI and CIRS were used

as the comorbidity indices. RESULTS: A total of 106 patients with pancreatic cancer were included in the study. The median overall survival rate was 9.0 [95 % confidence interval (CI): 6.7-11.3] months. The median overall survival rate was found as 9.4 (95 % CI: 6.7-12.1) months in the patients whose CCI score was </= 2 and was found as 6.2 (95 % CI: 4.0-8.3) months in the patients with CCI scores >/= 3 (p = 0.05). The median overall survival rate was calculated as 9.8 (95 % CI: 6.3-13.4) months in the patients with CIRS scores </= 2 and was calculated as 8.3 (95 % CI: 6.0-10.6) months in the patients with CIRS scores >/= 3 (p = 0.51). When surgery, radiotherapy, grading, and CCI score were evaluated using multivariate analysis, it was observed that only the treatment modality had a significant effect on the survival rate. CONCLUSION: The results on the use of comorbidity indices are contradictory for the cancers with lower survival rates such as pancreatic cancer. New prognostic scales might be developed for this patient group by considering the side effects of chemotherapy.

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[163]

TÍTULO / TITLE: - Expression of SOX9 in Intraductal Papillary Mucinous Neoplasms of the Pancreas.

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

REVISTA / JOURNAL: - Pancreas. 2013 Nov 7.

●● Enlace al texto completo (gratuito o de pago)

1097/MPA.0b013e3182a70b2f

AUTORES / AUTHORS: - Meng F; Takaori K; Ito T; Masui T; Kawaguchi M; Kawaguchi Y; Uemoto S

INSTITUCIÓN / INSTITUTION: - From the *Division of Hepatobiliary-Pancreatic Surgery and Transplantation, Department of Surgery, Kyoto University Graduate School of Medicine, Kyoto, Japan; daggerDepartment of General Surgery, The First Affiliated Hospital of China Medical University, Shenyang, China; and double daggerDepartment of Clinical Application, Center for iPS Cell Research and Application, Kyoto University, Kyoto, Japan.

RESUMEN / SUMMARY: - OBJECTIVES: SRY (sex determining region Y) box 9 (SOX9) plays a key role in the embryologic development, differentiation, and maintenance of organs in the pancreas as well as progression of several kinds of tumors. The aim of the present study was to evaluate the expression and potential role of SOX9 in intraductal papillary mucinous neoplasms (IPMNs) of the pancreas. METHODS: The authors selected 27 pathological tissues from 19 IPMN cases to assess the expression of SOX9 by means of immunohistochemistry and analyzed the expression pattern of SOX9 with 78 lesions obtained from these tissues stained by SOX9. RESULTS: SOX9 was expressed in the normal pancreas, IPMN, and pancreatic ductal adenocarcinoma. SOX9-positive cells were confined to the lower portions of the papillary structures of IPMN. However, SOX9 was expressed in the entire epithelium once the neoplasms advanced to high-grade dysplasia and invasive carcinoma. The expression pattern of SOX9 was similar to that of CD44 in the normal pancreas and IPMN. Double staining of SOX9 and CD44 detected colocalization of SOX9 and CD44 in IPMN. CONCLUSIONS: Changes in the SOX9 expression pattern may be involved in the mechanisms of the malignant progression of IPMN.

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[164]
TÍTULO / TITLE: - Overexpression of Calreticulin Contributes to the Development and Progression of Pancreatic Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Cell Physiol. 2013 Nov 22. doi: 10.1002/jcp.24519.
●● Enlace al texto completo (gratuito o de pago) 1002/jcp.24519
AUTORES / AUTHORS: - Sheng W; Chen C; Dong M; Zhou J; Liu Q; Dong Q; Li F
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Gastrointestinal Surgery, The First Hospital, China Medical University, Shenyang, 110001, China.
RESUMEN / SUMMARY: - We studied the clinicopathological significance for Calreticulin (CRT) expression in pancreatic cancer (PC), and its functional relationship with other signaling genes (especially with p53) in regulating the biological behavior of PC cells. IHC, IF, IB and real-time PCR were used to detect CRT expression in PC, while transfection and drug intervention were used to investigate the functional relationship of CRT with other signaling genes. IHC showed both CRT and p53 expression was significantly increased in PC, compared to that in paired noncancerous pancreatic tissues ($P < 0.001$). High expression of CRT was positively associated with tumor UICC stage and lymph nodes metastasis ($P = 0.034$ and $P = 0.015$), and was an independent adverse prognostic indicator in patients with PC. No relationship was found between CRT and p53 expression in spearman's rank correlation test. Altered expression of CRT did not change p53, MDM2, pho-AKT, pho-p38 and pho-JNK expression, but had a specific regulation on pho-ERK. Meanwhile, CRT regulated cell proliferation, migration and invasion of PC cells in MEK/ERK pathway dependent manner. In addition, CRT knockdown significantly decreased pho-ERK expression and cell chemoresistance independent of activated p53 and caspase-3 related apoptosis in gemcitabine or oxaliplatin treated Capan-2 cells. Our study first demonstrated that overexpression of CRT contributed to the development and progression of PC through MEK/ERK signaling pathway but independent of p53. The interaction between CRT and MEK/ERK pathway might provide a new idea for revealing malignant biology and supplying new gene targeted chemotherapy of PC. J. Cell. Physiol. © 2013 Wiley Periodicals, Inc.

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[165]
TÍTULO / TITLE: - Two immune faces of pancreatic adenocarcinoma: possible implication for immunotherapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cancer Immunol Immunother. 2013 Oct 16.
●● Enlace al texto completo (gratuito o de pago) 1007/s00262-013-1485-8
AUTORES / AUTHORS: - Bazhin AV; Shevchenko I; Umansky V; Werner J; Karakhanova S
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, University of Heidelberg, Im Neuenheimer Feld 156, 69120, Heidelberg, Germany, alexandr.bazhin@med.uni-heidelberg.de.
RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive human neoplasms, having extremely poor prognosis with a 5-year survival rate of <1 % and a median survival of 6 months. In contrast to other malignancies, pancreatic cancer is highly resistant to chemotherapy and targeted

therapy. Therefore, new treatment options are urgently needed to improve the survival of patients with PDAC. Based on our data showing that patients with higher CD8+ T cell tumour infiltration exhibited prolonged overall and disease-free survival compared to patients with lower or without CD8+ T cell tumour infiltration, we suggested that immunotherapy could be a promising treatment option for PDAC. However, clinical data from the chemoradioimmunotherapy with interferon-alpha (IFN) trial did not point to an improved efficiency of chemoradiation combined with IFN as compared to chemoradiotherapy alone, suggesting an important role of the immune suppression induced by PDAC and/or unspecific immune stimulation. In support of this hypothesis, we found that the PDAC patients and experimental mice had an increased number of regulatory T cells and myeloid-derived suppressor cells. These results allowed us to conclude that PDAC provokes not only an anti-tumour immune response, but also strong immune suppression. Thus, we supposed that new immunotherapeutical strategies should involve not only stimulation of the immune system of PDAC patients, but also exert control over the tumour immune suppressive milieu.

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[166]

TÍTULO / TITLE: - Diffusion-weighted MRI: usefulness for differentiating intrapancreatic accessory spleen and small hypervascular neuroendocrine tumor of the pancreas.

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

REVISTA / JOURNAL: - Acta Radiol. 2013 Nov 20.

●● Enlace al texto completo (gratuito o de pago) 1177/0284185113513760

AUTORES / AUTHORS: - Kang BK; Kim JH; Byun JH; Lee SS; Kim HJ; Kim SY; Lee MG

INSTITUCIÓN / INSTITUTION: - Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea.

RESUMEN / SUMMARY: - BACKGROUND: Image findings of intrapancreatic accessory spleen (IPAS) can closely resemble those of neuroendocrine tumor (NET) of the pancreas. PURPOSE: To investigate the usefulness of diffusion-weighted imaging (DWI) for differentiating IPAS from small (</=3 cm) hypervascular NET of the pancreas. MATERIAL AND METHODS: The visually assessed signal intensity of pancreatic lesions compared with the spleen on DWI (b value of 1000 s/mm2) and the apparent diffusion coefficient (ADC) values were compared in 25 patients with IPAS and 31 patients with small hypervascular NET. Two blinded radiologists independently rated their confidence in differentiating the two conditions and compared the diagnostic performance of contrast-enhanced magnetic resonance imaging (CE-MRI) alone with that of combined CE-MRI and DWI. RESULTS: The isointensity of the pancreatic lesions compared with the spleen on DWI was more frequently observed in IPAS than in NET (92% vs. 12.9%, P < 0.001). The mean ADC value was significantly lower in IPAS than in NET (0.90 x 10-3 mm2/s vs. 1.44 x 10-3 mm2/s, P < 0.001). The sensitivity and specificity of ADC quantification for differentiating the two conditions when using 1.07 x 10-3 mm2/s as the cut-off value were 96% and 93.5%, respectively. For both readers, the area under the receiver operating characteristic curve and accuracy in differentiating the two conditions of combined CE-MRI and DWI were significantly greater than those of CE-MRI alone (P </= 0.039). CONCLUSION: Visual

assessment of DWI and ADC quantification were useful in differentiating IPAS from small hypervascular NET of the pancreas.

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[167]
TÍTULO / TITLE: - Overview of the Pancreatic Toxicity and Carcinogenesis Session.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Toxicol Pathol. 2013 Oct 24.
●● Enlace al texto completo (gratuito o de pago) 1177/0192623313505931
AUTORES / AUTHORS: - Pandiri AR; Schultze AE
INSTITUCIÓN / INSTITUTION: - 1Experimental Pathology Laboratories, Inc., Research Triangle Park, North Carolina, USA.
RESUMEN / SUMMARY: - The theme of the Society of Toxicologic Pathology Annual Symposium 2013 was “Toxicologic Pathology of the Digestive Tract and Pancreas.” The last session focused on pancreatic toxicity and carcinogenesis. This overview highlights the various presentations in this session, focusing on pancreatic toxicologic pathology, responses of the pancreas to xenobiotics, and current understanding on pancreatic carcinogenesis. The objective of this symposium overview and the subsequent articles from this session is to enable the audience to develop a better appreciation for the pancreas as a target organ in toxicological studies.

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[168]
TÍTULO / TITLE: - Value of peritoneal cytology in potentially resectable pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Br J Surg. 2013 Dec;100(13):1791-6. doi: 10.1002/bjs.9307.
●● Enlace al texto completo (gratuito o de pago) 1002/bjs.9307
AUTORES / AUTHORS: - Yamada S; Fujii T; Kanda M; Sugimoto H; Nomoto S; Takeda S; Nakao A; Kodera Y
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery (Surgery II), Nagoya University Graduate School of Medicine, Nagoya, Japan.
RESUMEN / SUMMARY: - BACKGROUND: Peritoneal lavage cytology (CY) is used in the diagnosis and staging of various cancers. The clinical significance of positive cytology results in patients with pancreatic cancer is yet to be determined. METHODS: Peritoneal washing samples were collected from consecutive patients with pancreatic cancer between July 1991 and December 2012. The correlations between cytology results, clinicopathological parameters and recurrence patterns were evaluated. The prognostic impact of CY status, regarding resectability and the effectiveness of adjuvant chemotherapy, were analysed. RESULTS: Of 523 included patients, 390 underwent resection. Patients with tumours at least 2 cm in diameter were more likely to have CY+ status than patients with tumours smaller than 2 cm (48 of 312 versus 3 of 78 respectively; P = 0.005) and there was a significant correlation between CY+ status and tumour invasion of the anterior pancreatic capsule (43 of 276 versus 8 of 113 with no invasion of the capsule; P = 0.030). Although the overall survival of patients with resected CY+ tumours was worse than that of patients with resected CY- tumours, it was significantly better than the survival of unresected patients regardless of CY status. Multivariable analysis of all patients who had pancreatectomy did not identify

CY+ as an independent prognostic factor. Patients with CY+ tumours tended to develop peritoneal metastasis more often than those with CY- tumours, although not significantly so. The median survival time of 34 patients with resected CY+ tumours who received adjuvant chemotherapy was better than that of 17 patients who had surgery alone, although this was not statistically significant (15.3 versus 10.0 months; P = 0.057). CONCLUSION: CY+ status is not clinically equivalent to gross peritoneal metastasis in patients with pancreatic cancer. Curative resection is still recommended regardless of CY status. Presented to the 98th Annual Clinical Congress of the American College of Surgeons, Chicago, Illinois, USA, October 2012.

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[169]

TÍTULO / TITLE: - Transient interhemispheric disconnection in a case of insulinoma-induced hypoglycemic encephalopathy.

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

REVISTA / JOURNAL: - J Neurol Sci. 2013 Dec 15;335(1-2):233-7. doi: 10.1016/j.jns.2013.09.025. Epub 2013 Sep 25.

●● Enlace al texto completo (gratuito o de pago) 1016/j.jns.2013.09.025

AUTORES / AUTHORS: - Yamashita C; Shigeto H; Maeda N; Kawaguchi M; Uryu M; Motomura S; Kira J

INSTITUCIÓN / INSTITUTION: - Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Japan.

RESUMEN / SUMMARY: - We report a case of a 22-year-old male who was transferred to our hospital in a comatose state following successive seizures. Low blood glucose had been detected upon his arrival at the previous hospital. He became responsive 12days after the onset of coma. Upon regaining consciousness he exhibited severe dysarthria and several interhemispheric disconnection signs such as intermanual conflict, left-hand dysgraphia, left hemispatial neglect confined to the right hand, impaired interhemispheric transfer, and unilateral constructional apraxia of the right hand. Brain MRI disclosed T2-weighted and diffusion-weighted hyperintense lesions with reduced apparent diffusion coefficients in the bilateral centrum semiovale, splenium of the corpus callosum, right posterior limb of the internal capsule, and bilateral middle cerebellar peduncles. As the MRI findings vanished, his interhemispheric disconnection signs gradually resolved. Abdominal imaging studies revealed a pancreatic tumor, which was later endocrinologically diagnosed as an insulinoma. This is an extremely rare report of interhemispheric disconnection signs due to hypoglycemic encephalopathy. The lesions in the bilateral centrum semiovale likely contributed to the interhemispheric disconnection signs.

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[170]

TÍTULO / TITLE: - Molecular determinants of susceptibility to oncolytic vesicular stomatitis virus in pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - J Surg Res. 2013 Oct 21. pii: S0022-4804(13)00977-3. doi: 10.1016/j.jss.2013.10.032.

●● Enlace al texto completo (gratuito o de pago) 1016/j.jss.2013.10.032

AUTORES / AUTHORS: - Blackham AU; Northrup SA; Willingham M; Sirintrapun J; Russell GB; Lyles DS; Stewart JH 4th

INSTITUCIÓN / INSTITUTION: - Division of Surgical Sciences, Department of General Surgery, Wake Forest School of Medicine, Winston-Salem, North Carolina.

RESUMEN / SUMMARY: - BACKGROUND: M protein mutant vesicular stomatitis virus (M51R-VSV) has oncolytic properties against many cancers. However, some cancer cells are resistant to M51R-VSV. Herein, we evaluate the molecular determinants of vesicular stomatitis virus (VSV) resistance in pancreatic adenocarcinoma cells. METHODS: Cell viability and the effect of beta-interferon (IFN) were analyzed using 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetr azolium assay. Gene expression was evaluated via microarray analysis. Cell infectability was measured by flow cytometry. Xenografts were established in athymic nude mice and treated with intratumoral M51R-VSV. RESULTS: Four of five pancreatic cancer cell lines were sensitive to M51R-VSV, whereas Panc 03.27 cells remained resistant (81 +/- 3% viability 72 h after single-cycle infection). Comparing sensitive MiaPaCa2 cells with resistant Panc 03.27 cells, significant differences in gene expression were found relating to IFN signaling (P = 2 x 10-5), viral entry (P = 3 x 10-4), and endocytosis (P = 7 x 10-4). MiaPaCa2 cells permitted high levels of VSV infection, whereas Panc 03.27 cells were capable of resisting VSV cell entry even at high multiplicities of infection. Extrinsic beta-IFN overcame apparent defects in IFN-mediated pathways in MiaPaCa2 cells conferring VSV resistance. In contrast, beta-IFN decreased cell viability in Panc 3.27 cells, suggesting intact antiviral mechanisms. VSV-treated xenografts exhibited reduced tumor growth relative to controls in both MiaPaCa2 (1423 +/- 345% versus 164 +/- 136%; P < 0.001) and Panc 3.27 (979 +/- 153% versus 50 +/- 56%; P = 0.002) tumors. Significant lymphocytic infiltration was seen in M51R-VSV-treated Panc 03.27 xenografts. CONCLUSIONS: Inhibition of VSV endocytosis and intact IFN-mediated defenses are responsible for M51R-VSV resistance in pancreatic adenocarcinoma cells. M51R-VSV treatment appears to induce antitumor cellular immunity in vivo, which may expand its clinical efficacy.

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[171]

TÍTULO / TITLE: - Importance of b value in diffusion weighted imaging for the diagnosis of pancreatic cancer.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Oct 21;19(39):6651-5. doi: 10.3748/wjg.v19.i39.6651.

●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i39.6651

AUTORES / AUTHORS: - Hao JG; Wang JP; Gu YL; Lu ML

INSTITUCIÓN / INSTITUTION: - Jin-Gang Hao, Jia-Ping Wang, Ya-Lv Gu, Department of Radiology, the Second Affiliated Hospital of Kunming Medical University, Kunming 650101, Yunnan Province, China.

RESUMEN / SUMMARY: - AIM: To investigate the use of multi-b-value diffusion-weighted imaging in diagnosing pancreatic cancer. METHODS: We retrospectively analyzed 33 cases of pancreatic cancer and 12 cases of benign pancreatic tumors at the Second Affiliated Hospital of Kunming Medical University from December 2008 to January 2011. The demographic characteristics, clinical presentation, routine magnetic resonance imaging and diffusion weighted imaging (DWI) features with different b

values were reviewed. Continuous data were expressed as mean +/- SD. Comparisons between pancreatic cancer and benign pancreatic tumors were performed using the Student's t test. A probability of P < 0.05 was considered statistically significant. RESULTS: Thirty-three patients with pancreatic cancer were identified. The mean age at diagnosis was 60 +/- 5.6 years. The male: female ratio was 21:12. Twenty cases were confirmed by surgical resection and 13 by biopsy of metastases. T1 weighted images demonstrated a pancreatic head mass in 16 patients, a pancreatic body mass in 10 cases, and a pancreatic tail mass with pancreatic atrophy in 7 cases. Eight patients had hepatic metastases, 13 had invasion or envelopment of mesenteric vessels, 4 had bone metastases, and 8 had lymph node metastases. DWI demonstrated an irregular intense mass with unclear margins. Necrotic tissue demonstrated an uneven low signal. A b of 1100 s/mm(2) was associated with a high intensity signal with poor anatomical delineation. A b of 700 s/mm(2) was associated with apparent diffusion coefficients (ADCs) that were useful in distinguishing benign and malignant pancreatic tumors (P < 0.05). b values of 50, 350, 400, 450 and 1100 s/mm(2) were associated with ADCs that did not differentiate the two tumors. CONCLUSION: Low b value images demonstrated superior anatomical details when compared to high b value images. Tumor tissue definition was high and contrast with the surrounding tissues was good. DWI was useful in diagnosing pancreatic cancer.

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[172]

TÍTULO / TITLE: - Value of near-isovoxel ultrasound for evaluation of ductal communications with pancreatic cystic lesions: correlation with magnetic resonance cholangiopancreatography.

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

REVISTA / JOURNAL: - Ultrasound Med Biol. 2013 Dec;39(12):2279-84. doi: 10.1016/j.ultrasmedbio.2013.07.011. Epub 2013 Oct 16.

●● Enlace al texto completo (gratuito o de pago)

1016/j.ultrasmedbio.2013.07.011

AUTORES / AUTHORS: - Yu MH; Lee JY; Kim JH; Han JK; Choi BI

INSTITUCIÓN / INSTITUTION: - Department of Radiology and Institute of Radiation Medicine, Seoul National University Hospital, Seoul, Korea.

RESUMEN / SUMMARY: - The aim of this study was to determine the value of near-isovoxel ultrasound (ISUS) using xMATRIX technology in assessment of ductal communications with pancreatic cystic lesions. Twenty patients with pancreatic cystic lesions (n = 21) on magnetic resonance cholangiopancreatography (MRCP), underwent 2-D ultrasound (US) and subsequent ISUS using a matrix probe. Two observers assessed the presence of ductal communications with pancreatic cystic lesions for all MRCP, 2-D US, and ISUS images with multi-planar reformation, using a 5-point confidence scale. Weighted-kappa statistics and intra-class correlation coefficients were calculated. Inter-observer agreement for MRCP, 2-D US and ISUS was moderate, fair and moderate (0.475, 0.222 and 0.472), respectively. The intra-class correlation coefficients between ISUS and MRCP was higher than that between 2-D US and MRCP (0.8706 vs. 0.5353, observer 1; 0.7206 vs. 0.4818, observer 2, respectively). Correlation and inter-observer agreement were better with MRCP than with 2-D US. We conclude that ISUS may be useful in evaluating ductal communications with pancreatic cystic lesions.

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[173]

TÍTULO / TITLE: - Oncological Feasibility of Laparoscopic Distal Pancreatectomy for Adenocarcinoma: A Single-Institution Comparative Study.

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

REVISTA / JOURNAL: - World J Surg. 2013 Oct 1.

●● Enlace al texto completo (gratuito o de pago) 1007/s00268-013-2268-2

AUTORES / AUTHORS: - Rehman S; John SK; Lochan R; Jaques BC; Manas DM; Charnley RM; French JJ; White SA

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary and Transplantation Surgery, Freeman Hospital, Freeman Road, High Heaton, Newcastle upon Tyne, NE7 7DN, UK, Srkhanswati75@yahoo.com.

RESUMEN / SUMMARY: - BACKGROUND: Laparoscopic distal pancreatectomy (LDP) is performed increasingly for pancreatic pathology in the body and tail of the pancreas. However, only few reports have compared its oncological efficacy with open distal pancreatectomy (ODP). We compared these two techniques in patients with pancreatic ductal adenocarcinoma. METHODS: From a prospectively maintained database, all patients who underwent either LDP or ODP for adenocarcinoma in the body and tail of the pancreas between January 2008 and December 2011 were compared. Data were analysed using SPSS® v19 utilising standard tests. A p value <0.05 was considered significant. RESULTS: Of 101 patients who underwent distal pancreatectomy, 22 had histologically confirmed adenocarcinoma (LDP n = 8, ODP n = 14). Both groups were well matched for age and the size of tumour (22 vs. 32 mm, p = 0.22). Intraoperative blood loss was 306 ml compared with 650 ml for ODP (p = 0.152). A longer operative time was noted for LDP (376 vs. 274 min, p < 0.05). Total length of stay was shorter for LDP compared with ODP (8 vs. 12 days, p = 0.05). The number of postoperative pancreatic fistulas were similar (LDP n = 2 vs. ODP n = 3, p = 0.5). Complete resection (R0) was achieved in 88 % of LDP (n = 7) compared with 86 % of ODP (n = 12). The median number of lymph nodes harvested was 16 for LDP versus 14 for ODP. Overall 3-year survival also was similar: LDP = 82 %, ODP = 74 % (p = 0.89). CONCLUSIONS: From an oncological perspective, LDP is a viable procedure and its results are comparable to ODP for ductal adenocarcinomas arising in the body and tail of the pancreas.

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[174]

TÍTULO / TITLE: - Extracapsular Lymph Node Spread as a Negative Prognostic Factor of Adenocarcinoma of the Pancreas and Cancer of the Papilla of Vater.

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

REVISTA / JOURNAL: - Pancreas. 2013 Nov 7.

●● Enlace al texto completo (gratuito o de pago) 1097/MPA.0b013e3182a44a91

AUTORES / AUTHORS: - Prenzel KL; Holscher AH; Drebber U; Bollschweiler E; Gutschow CA; Stippel DL; Monig SP

INSTITUCIÓN / INSTITUTION: - From the Department of General, Visceral and Cancer Surgery, and Institute of Pathology, University of Cologne, Cologne, Germany.

RESUMEN / SUMMARY: - OBJECTIVE: The aim of this study was to analyze the incidence and impact of extracapsular lymph node spread (ELNS) in pancreatic cancer (PC) and cancer of the papilla of Vater (CPV). METHODS: Between 2004 and 2009, 148 patients underwent surgical therapy for PC (n = 112) and CPV (n = 36). The resected lymph nodes (LNs) were further analyzed for ELNS. RESULTS: In 95 (64.2%) patients, LN metastasis was present. In 45 (47.3%) of these patients, an ELNS was present on histopathology. The patients' survival was negatively affected by ELNS. For PC, the 5-year survival rate was 37% for patients with no LN metastasis compared with 4% and 0% for patients with LN metastasis (pN1) but without extracapsular LN involvement and patients with pN1 disease with extracapsular LN involvement of at least 1 LN, respectively (P < 0.001). In patients with CPV, the 5-year survival rate was 56% for patients with no LN metastasis and 44% and 0% for patients with pN1 disease but without extracapsular LN involvement and patients with pN1 disease with extracapsular LN involvement of at least 1 LN, respectively (P = 0.006). Multivariate analysis revealed ELNS as an independent prognostic factor of survival for both tumor types. CONCLUSIONS: Extracapsular LN spread is an independent negative prognostic factor in PC and CPV. In future staging systems, ELNS should be included.

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[175]

TÍTULO / TITLE: - Repeat pancreatectomy for pancreatic ductal cancer recurrence in the remnant pancreas after initial pancreatectomy: Is it worthwhile?

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

REVISTA / JOURNAL: - Surgery. 2013 Nov 12. pii: S0039-6060(13)00372-3. doi: 10.1016/j.surg.2013.06.050.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.06.050

AUTORES / AUTHORS: - Miyazaki M; Yoshitomi H; Shimizu H; Ohtsuka M; Yoshidome H; Furukawa K; Takayasiki T; Kuboki S; Okamura D; Suzuki D; Nakajima M

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan. Electronic address: masaru@faculty.chiba-u.jp.

RESUMEN / SUMMARY: - BACKGROUND: The clinical implications of repeat completion pancreatectomy for recurrent pancreatic cancer in the remnant pancreas after initial pancreatectomy have not been clarified. We retrospectively analyzed our patients and evaluated the clinical implications of repeat pancreatectomy for isolated local recurrence in the remnant pancreas after initial resection for pancreatic cancer. METHODS: One-hundred seventy patients who had recurrence of pancreatic cancer out of 326 patients who had initially undergone resection for pancreatic cancer were included in this study. Sixty-seven of 170 recurrent patients were diagnosed as having isolated local recurrence of pancreatic cancer. Eleven of these 67 patients with isolated local recurrence only in the remnant pancreas underwent repeat pancreatectomy. Characteristics and operative outcomes for these 11 patients with repeat pancreatectomy were analyzed and evaluated in comparison with other recurrent patients. RESULTS: Among 170 patients with recurrence after initial resection for pancreatic cancer, the median survival time was 78.2 and 20.3 months after initial resection, in the repeat pancreatectomy group and the unresectable group, respectively (P < .001), and the 2- and 5-year survival probability rates after initial resection were 91%, and 82% vs 42%, and 13%, respectively. Among 67 patients with

isolated local recurrence, the median survival time after repeat resection or diagnosis of recurrence was 25.0 and 9.3 months, and the 2- and 5-year survival probability rates after repeat resection or diagnosis of recurrence were and 61% and 46% vs 19% and 6.2% in the repeat pancreatectomy group and the unresectable group, respectively (P < .01). There was no difference in survivals between the unresectable isolated local recurrence group and the unresectable nonlocal recurrence group. CONCLUSION: Repeat pancreatectomy might bring about beneficial effects on prognosis in selected patients with isolated local recurrence in the remnant pancreas after initial pancreatectomy for pancreatic cancer without increased operative morbidity or mortality.

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[176]

TÍTULO / TITLE: - Predicting aggressive behavior in nonfunctioning pancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - Surgery. 2013 Oct;154(4):785-91; discussion 791-3. doi: 10.1016/j.surg.2013.07.004.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.07.004

AUTORES / AUTHORS: - Cherenfant J; Stocker SJ; Gage MK; Du H; Thurow TA; Odeleye M; Schimpke SW; Kaul KL; Hall CR; Lamzabi I; Gattuso P; Winchester DJ; Marsh RW; Roggin KK; Bentrem DJ; Baker MS; Prinz RA; Talamonti MS

INSTITUCIÓN / INSTITUTION: - NorthShore University HealthSystems, Evanston, IL. Electronic address: jovenel1@yahoo.com.

RESUMEN / SUMMARY: - PURPOSE: The biologic potential of nonfunctioning pancreatic neuroendocrine tumors (PNETs) is highly variable and difficult to predict before resection. This study was conducted to identify clinical and pathologic factors associated with malignant behavior and death in patients diagnosed with PNETs. METHODS: We used International Classification of Diseases 9th edition codes to identify patients who underwent pancreatectomy for PNETs from 1998 to 2011 in the databases of 4 institutions. Functioning PNETs were excluded. Multivariate regression Cox proportional models were constructed to identify clinical and pathologic factors associated with distant metastasis and survival. RESULTS: The study included 128 patients-57 females and 71 males. The age (mean +/- standard deviation) was 55 +/- 14 years. The body mass index was 28 +/- 5 kg/m(2). Eighty-nine (70%) patients presented with symptoms, and 39 (30%) had tumors discovered incidentally. The tumor size was 3.3 +/- 2 cm with 56 (44%) of the tumors measuring </=2 cm. Seventy-three (57%) patients had grade 1 histology tumors, 37 (29%) had grade 2, and 18 (14%) had grade 3. Peripancreatic lymph node involvement was present in 31 patients (24%), absent in 75 (59%), and unknown in 22 (17%). Distant metastasis occurred in 18 patients (14%). There were 12 deaths, including 1 perioperative, 8 disease related, and 3 of unknown cause. With a median follow-up of 33 months, the overall 5-year survival was 75%. Multivariate Cox regression analysis identified age >55 (hazard ratio [HR], 5.89; 95% confidence interval [CI], 1.64-20.58), grade 3 histology (HR, 6.08; 95% CI, 1.32-30.2), and distant metastasis (HR, 8.79; 95% CI, 2.67-28.9) as risk factors associated with death (P < .05). Gender, race, body mass index, clinical symptoms, lymphovascular and perineural invasion, and tumor size were not related to metastasis or survival (P > .05). Three patients with tumors </=2 cm developed distant metastasis

resulting in 2 disease-related deaths. CONCLUSION: Age >55 years, grade 3 histology, and distant metastasis predict a greater risk of death from nonfunctioning PNETs. Resection or short-term surveillance should be considered regardless of tumor size.

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[177]
TÍTULO / TITLE: - Pathogenesis of Pancreatic Cancer: Lessons from Animal Models.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Toxicol Pathol. 2013 Oct 31.
●● Enlace al texto completo (gratuito o de pago) 1177/0192623313508250
AUTORES / AUTHORS: - Murtaugh LC
INSTITUCIÓN / INSTITUTION: - 1Department of Human Genetics, University of Utah, Salt Lake City, Utah, USA.
RESUMEN / SUMMARY: - The past several decades have seen great effort devoted to mimicking the key features of pancreatic ductal adenocarcinoma (PDAC) in animals and have produced 2 robust models of this deadly cancer. Carcinogen-treated Syrian hamsters develop PDAC with genetic lesions, which reproduce those of human, including activation of the Kras oncogene, and early studies in this species validated nongenetic risk factors for PDAC including pancreatitis, obesity, and diabetes. More recently, PDAC research has been invigorated by the development of genetically engineered mouse models based on tissue-specific Kras activation and deletion of tumor suppressor genes. Surprisingly, mouse PDAC appears to arise from exocrine acinar rather than ductal cells, via a process of phenotypic reprogramming that is accelerated by inflammation. Studies in both models have uncovered molecular mechanisms by which inflammation promotes and sustains PDAC and identified targets for chemoprevention to suppress PDAC in high-risk individuals. The mouse model, in particular, has also been instrumental in developing new approaches to early detection as well as treatment of advanced disease. Together, animal models enable diverse approaches to basic and preclinical research on pancreatic cancer, the results of which will accelerate progress against this currently intractable cancer.

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[178]
TÍTULO / TITLE: - Minimally-Invasive vs Open Pancreaticoduodenectomy: Systematic Review and Meta-Analysis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Am Coll Surg. 2013 Nov 23. pii: S1072-7515(13)01073-9. doi: 10.1016/j.jamcollsurg.2013.09.005.
●● Enlace al texto completo (gratuito o de pago)
1016/j.jamcollsurg.2013.09.005
AUTORES / AUTHORS: - Correa-Gallego C; Dinkelspiel HE; Sulimanoff I; Fisher S; Vinuela EF; Kingham TP; Fong Y; Dematteo RP; D'Angelica MI; Jarnagin WR; Allen PJ
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.

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[179]

TÍTULO / TITLE: - Efficient targeting and tumor retardation effect of pancreatic adenocarcinoma up-regulated factor (PAUF)-specific RNA replacement in pancreatic cancer mouse model.

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

REVISTA / JOURNAL: - Cancer Lett. 2013 Nov 1. pii: S0304-3835(13)00783-0. doi: 10.1016/j.canlet.2013.10.028.

●● Enlace al texto completo (gratuito o de pago) 1016/j.canlet.2013.10.028

AUTORES / AUTHORS: - Kim YH; Moon JY; Kim EO; Lee SJ; Kang SH; Kim SK; Heo K; Lee Y; Kim H; Kim KT; Kim D; Song MS; Lee SW; Lee Y; Koh SS; Kim IH

INSTITUCIÓN / INSTITUTION: - Research Institute & Hospital, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang-si, Gyeonggi-do 410-769, Republic of Korea. Electronic address: sensia37@ncc.re.kr.

RESUMEN / SUMMARY: - The soluble protein pancreatic adenocarcinoma up-regulated factor (PAUF) plays an important role in pancreatic tumor progression and has begun to attract attention as a therapeutic target for pancreatic cancer. We herein present PAUF RNA-targeting gene therapy strategies with both targeting and therapeutic function using trans-splicing ribozyme (TSR) in pancreatic cancer. We developed adenoviral PAUF-targeting TSR (Rz) containing a PAUF-specific internal guide sequence (IGS) determined by library screening. This Rz harbors suicide gene, herpes simplex virus thymidine kinase (HSV-tk) or firefly luciferase (Luc) as a transgene for 3' exon replacement of PAUF RNAs. Ad-Rz-TK, Rz harboring the HSV-tk, showed significant inhibition of tumor growth in vivo as well as PAUF-dependent cell death in vitro via a successful trans-splicing reaction. Selective induction of Rz-controlled transgene in PAUF-expressing pancreatic cancer was confirmed through noninvasive in vivo imaging; a luminescence signal from Rz harboring Luc (Ad-Rz-Luc) was detectable only in pancreatic tumor sites, not in normal mice. In addition, a [125I] FIAU signal reflecting thymidine kinase expression through SPECT and ex vivo biodistribution was co-localized with the tumor sites when we treated with Ad-Rz-TK in orthotopic xenograft model. Taken together, these results imply that PAUF-targeting TSR can contribute to successful targeted gene therapy for pancreatic cancer.

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[180]

TÍTULO / TITLE: - Prognostic Factors for Successful Endoscopic Transpapillary Drainage of Pancreatic Pseudocysts.

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

REVISTA / JOURNAL: - Dig Dis Sci. 2013 Nov 2.

●● Enlace al texto completo (gratuito o de pago) 1007/s10620-013-2924-2

AUTORES / AUTHORS: - Lin H; Zhan XB; Jin ZD; Zou DW; Li ZS

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Shanghai 10th People's Hospital, Tongji University School of Medicine, Shanghai, 200072, China.

RESUMEN / SUMMARY: - BACKGROUND AND AIMS: The transpapillary approach can be used for draining pancreatic pseudocysts (PPs) with pancreatic-duct abnormalities. The purpose of this study was to analyze prognostic factors for clinical success of transpapillary drainage. PATIENTS AND METHODS: Data for all patients who underwent transpapillary drainage between November 2000 and September 2009 were obtained by retrospective review and entered into a computerized database. Patient data were prospectively followed up to determine long-term outcomes. RESULTS:

Seventy interventional ERCP procedures were performed for 43 patients. Technical success was 90.7 % (39/43). Overall clinical success was 79.5 % (31/39). Clinical success for pancreatic head pseudocyst was significantly different from that for body or tail pseudocyst (62.5 vs. 91.3 %, P = 0.043). Logistic regression analysis showed that location of the PPs predicted the success of endoscopic transpapillary pseudocyst drainage (P = 0.025). CONCLUSION: Transpapillary drainage is the least traumatic approach for drainage of PPs, and is also effective for patients with no communicating pseudocysts. Clinical success for pancreatic body or tail pseudocyst drainage was higher than that for pancreatic head pseudocyst drainage. It was found that the location of PPs predicted the success of transpapillary pseudocyst drainage. None of the other factors tested was a significant predictor of clinical success.

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[181]

TÍTULO / TITLE: - Synthetic alpha-(aminomethyl)-gamma-butyrolactones and their anti-pancreatic cancer activities.

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

REVISTA / JOURNAL: - Bioorg Med Chem Lett. 2013 Dec 15;23(24):6911-4. doi: 10.1016/j.bmcl.2013.09.065. Epub 2013 Sep 30.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bmcl.2013.09.065

AUTORES / AUTHORS: - Ramachandran PV; Nicponski DR; Nair HN; Helppi MA; Gagare PD; Schmidt CM; Yip-Schneider MT

INSTITUCIÓN / INSTITUTION: - Herbert C. Brown Center for Borane Research, Department of Chemistry, Purdue University, 560 Oval Drive, West Lafayette, IN 47907-2084, USA. Electronic address: chandran@purdue.edu.

RESUMEN / SUMMARY: - Aminated alpha-methylene-gamma-butyrolactones, which are readily synthesized with facile control of the diastereoisomerism, provide an economical and commercially-viable alternative to the use of aminated natural products. These aminoloactones, which exhibit excellent activity against three pancreatic cancer cell lines when measured at 10muM-Panc-1, MIA PaCa-2, and BxPC-3-and are comparable to or better than parthenolide and dimethylaminoparthenolide (DMAPT, LC-1). It has also been shown that there is an effect on the biological activity depending on the identity of the amine.

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[182]

TÍTULO / TITLE: - Phospho-sulindac inhibits pancreatic cancer growth: NFATc1 as a drug resistance candidate.

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

REVISTA / JOURNAL: - Int J Oncol. 2013 Nov 27. doi: 10.3892/ijo.2013.2190.

●● Enlace al texto completo (gratuito o de pago) 3892/ijo.2013.2190

AUTORES / AUTHORS: - Murray OT; Wong CC; Vrankova K; Rigas B

INSTITUCIÓN / INSTITUTION: - Division of Cancer Prevention, Department of Medicine, Stony Brook University, Stony Brook, NY 11794-8173, USA.

RESUMEN / SUMMARY: - Phospho-sulindac (P-S), a promising anticancer agent, is efficacious in pre-clinical models of human cancer and is apparently safe. Here, we studied the effect of P-S on pancreatic cancer growth. We found that P-S strongly inhibits the growth of human pancreatic cancer cells in vitro, is efficacious in inhibiting

the growth of pancreatic xenografts in nude mice, and has an excellent safety profile. Microarray analysis revealed that P-S induced the expression of nuclear factor of activated T-cells, isoform c1 (NFATc1) gene. NFATc1, a calcineurin-responsive transcription factor associated with aggressive pancreatic cancer. The role of increased NFATc1 expression on the growth inhibitory effect of P-S on cancer growth was evaluated by silencing or by overexpressing it both in vitro and in vivo. We found that when the expression of NFATc1 was abrogated by RNAi, pancreatic cancer cells were more responsive to treatment with P-S. Conversely, overexpressing the NFATc1 gene made the pancreatic cancer cells less responsive to treatment with P-S. NFATc1 likely mediates drug resistance to P-S and is an unfavorable prognostic factor that predicts poor tumor response. We also demonstrated that NFATc1-mediated resistance can be overcome by cyclosporin A (CsA), an NFAT inhibitor, and that the combination of P-S and CsA synergistically inhibited pancreatic cancer cell growth. In conclusion, our preclinical data establish P-S as an efficacious drug for pancreatic cancer in preclinical models, which merits further evaluation.

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[183]

TÍTULO / TITLE: - hsa-miR-141 downregulates TM4SF1 to inhibit pancreatic cancer cell invasion and migration.

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

REVISTA / JOURNAL: - Int J Oncol. 2013 Nov 27. doi: 10.3892/ijo.2013.2189.

●● Enlace al texto completo (gratuito o de pago) 3892/ijo.2013.2189

AUTORES / AUTHORS: - Xu L; Li Q; Xu D; Wang Q; An Y; Du Q; Zhang J; Zhu Y; Miao Y

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, The Second Affiliated Hospital of Nanjing Medical University, Nanjing 210018, P.R. China.

RESUMEN / SUMMARY: - Expression of the transmembrane-4-L-six-family-1 (TM4SF1) is high in human pancreatic cancer cells, but the underlying mechanism remains unclear. In this study, we aimed to identify and characterize microRNAs that regulate TM4SF1 expression in PC cells. Western blot analysis and quantitative polymerase chain reaction were used to detect TM4SF1 and hsa-miR-141 levels in four PC cell lines. SW1990 and BxPc-3 cells were transfected with the inhibitor miR-141, the inhibitor negative control, the miR-141 mimic and the mimic negative control; and cell invasion, migration, proliferation, cell cycle progression and apoptosis were detected by Transwell, MTT and flow cytometry assays, respectively. The miR-141 levels negatively correlated with the TM4SF1 protein levels in PC cells. The TM4SF1 protein levels were lower in the 141M group but higher in the 141I group, although the TM4SF1 mRNA levels had no significant changes, compared to the negative controls. Luciferase assays demonstrated that hsa-miR-141 directly targeted the 3'-untranslated region of the TM4SF1 gene. In addition, miR-141 downregulated TM4SF1 expression to inhibit invasion and migration of PC cells but had no effects on cell proliferation, cell cycle progression or apoptosis. TM4SF1 is a direct target of miR-141. Our findings that TM4SF1 expression was inhibited by miR-141 provide new insights into the oncogenic mechanism of TM4SF1 and suggest that miR-141 represents a novel molecular target for PC therapy.

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[184]
TÍTULO / TITLE: - Antiproliferation activity of Devil's club (Oplopanax horridus) and anticancer agents on human pancreatic cancer multicellular spheroids.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Phytomedicine. 2013 Nov 8. pii: S0944-7113(13)00401-7. doi: 10.1016/j.phymed.2013.10.003.
●● Enlace al texto completo (gratuito o de pago) 1016/j.phymed.2013.10.003
AUTORES / AUTHORS: - Tai J; Cheung SS; Ou D; Warnock GL; Hasman D
INSTITUCIÓN / INSTITUTION: - Department of Pathology and Laboratory Medicine, Child and Family Research Institute, University of British Columbia, Canada. Electronic address: jtai@mail.ubc.ca.
RESUMEN / SUMMARY: - Devil's club (DC, Oplopanax horridus) is an important medicinal herb of the Pacific Northwest which has significant antiproliferation activity against a variety of human tumor cell lines in vitro. This study compared the antiproliferation activity of DC extract alone, and in combination with chemotherapeutic agents gemcitabine (GEM), cisplatin (CDDP), and paclitaxel (PTX) on human pancreatic cancer PANC-1 3D spheroids and 2D monolayer cells. 3D tumor spheroids were prepared with a rotary cell culture system. PANC-1 3D spheroids were significantly more resistant to killing by DC extract, GEM and PTX compared to 2D cells, with IC50 levels closer to that observed in vivo. DC extract significantly enhanced the antiproliferation activity of CDDP and GEM at some concentrations. The bioactive compound identified as a polyacetylene showed strong antiproliferation activity against PANC-1 2D cells and 3D spheroids with IC50 at 0.73+/-0.04 and 3.15+/-0.16muM, respectively. 3D spheroids and 2D cells differentially expressed a number of apoptosis related genes. Cell cycle analysis showed that the proportion of cells in S phase was increased and in G2/M phase reduced in 3D spheroids compared to 2D cells. DC extract can potentially be used to enhance the activity of chemotherapeutic agents against pancreatic cancer cells. Use of 3D spheroid model for screening of natural products can potentially increase the efficiency in discovering in vivo bioactive compounds.

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[185]
TÍTULO / TITLE: - Pancreas-sparing duodenectomy for gastrointestinal stromal tumor.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Am J Surg. 2013 Oct 10. pii: S0002-9610(13)00456-X. doi: 10.1016/j.amjsurg.2013.05.009.
●● Enlace al texto completo (gratuito o de pago) 1016/j.amjsurg.2013.05.009
AUTORES / AUTHORS: - Yamashita S; Sakamoto Y; Saiura A; Yamamoto J; Kosuge T; Aoki T; Sugawara Y; Hasegawa K; Kokudo N
INSTITUCIÓN / INSTITUTION: - Hepato-Biliary-Pancreatic Surgery Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan.
RESUMEN / SUMMARY: - BACKGROUND: Pancreas-sparing duodenectomy (PSD) is a promising alternative procedure to pancreaticoduodenectomy for the treatment of duodenal tumors with low-grade malignant behavior. METHODS: Between March 2003 and September 2012, PSD was performed in 7 patients with a gastrointestinal stromal tumor (GIST) in the second (n = 5) or third (n = 2) portions of the duodenum. The short-

and long-term outcomes of treatment were analyzed in all patients. RESULTS: The median blood loss was 160 mL, and the median operative time was 315 minutes. No pancreatic leakage or perioperative mortality occurred. Surgical margins were negative in all cases. All patients were alive at the median follow-up time of 42 months after PSD. The recurrence-free 5-year survival rate was 53% in all patients. Hepatic metastases developed in 2 of the 5 patients with high- or intermediate-grade risks at the time of diagnosis. Hepatic resection was performed, and imatinib mesylate was administered in the 2 cases. CONCLUSIONS: Good short- and long-term outcomes and surgical curability were observed in patients treated with PSD for duodenal GIST.

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[186]

TÍTULO / TITLE: - An improved synthesis of 1'-[(18) F]fluoroethyl-beta-d-lactose ([(18) F]-FEL) for positron emission tomography imaging of pancreatic cancer.

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

REVISTA / JOURNAL: - J Labelled Comp Radiopharm. 2013 Jun 15;56(7):351-5. doi: 10.1002/jlcr.3042. Epub 2013 Mar 22.

●● Enlace al texto completo (gratuito o de pago) 1002/jlcr.3042

AUTORES / AUTHORS: - Turkman N; Gelovani JG; Alauddin MM

INSTITUCIÓN / INSTITUTION: - Department of Experimental Diagnostic Imaging, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA; Wayne state University, Detroit, MI, USA.

RESUMEN / SUMMARY: - INTRODUCTION: Earlier, we reported syntheses of ethyl-beta-d-galactopyranosyl-(1,4')-2'-deoxy-2'-[(18) F]fluoro-beta-d-glucopyranoside (Et-[(18) F]FDL) and 1'-[(18) F]fluoroethyl-beta-d-lactose ([(18) F]-FEL) for positron emission tomography (PET) of pancreatic carcinoma. Et-[(18) F]FDL requires a precursor, which involves 11 steps to synthesize and produces overall low yields. Synthesis of precursors for [(18) F]-FEL requires four steps, but those precursors produced low radiochemical yields. Here, we report new precursors and an improved synthesis of [(18) F]-FEL. METHOD: Two precursors, 1'-(methanesulfonyl)ethyl-2',3',6',2,3,4,6-hepta-O-acetyl-beta-d-lactose 2a and 1'-(p-nitrophenyl-sulfonyl)ethyl-2',3',6',2,3,4,6-hepta-O-acetyl-beta-d-lactose 2b, were synthesized from lactose in four steps. Radiofluorination reactions were performed using K(18) F/kryptofix and the crude product [(18) F]-3 was purified by HPLC. Basic hydrolysis of [(18) F]-3 produced 1'-[(18) F]fluoroethyl-beta-d-lactose [(18) F]-4, which was neutralized, diluted with saline, filtered on a 0.22-microm filter, and analyzed by radio-TLC. RESULTS: The average radiochemical yields of [(18) F]-4 (d. c.) from 2a and 2b were 21% (n = 6) and 65% (n = 6), respectively, with >99% radiochemical purity and specific activity of 55.5 GBq/micromol. Synthesis time was 90-95 min from the end of bombardment. CONCLUSION: An improved synthesis of [(18) F]FEL has been achieved in high yields, with high purity and specific activity. Precursor 2b with this method should be applicable for high yield automated production in a commercial synthesis module for clinical application.

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[187]

TÍTULO / TITLE: - Dual Inhibition of PI3K and mTOR Signaling Pathways Decreases Human Pancreatic Neuroendocrine Tumor Metastatic Progression.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreas. 2013 Nov 20.
●● Enlace al texto completo (gratuito o de pago)
1097/MPA.0b013e3182a44ab4
AUTORES / AUTHORS: - Djukom C; Porro LJ; Mrazek A; Townsend CM Jr; Hellmich MR; Chao C
INSTITUCIÓN / INSTITUTION: - From the Department of Surgery, University of Texas Medical Branch, Galveston, TX.
RESUMEN / SUMMARY: - OBJECTIVES: Patients with advanced pancreatic neuroendocrine tumors have limited therapeutic options. Everolimus (RAD001), an inhibitor of the mammalian target of rapamycin (mTOR) pathway, has been shown to increase progression-free survival, but not overall survival, indicating a need to identify additional therapeutic targets. Inhibition of mTOR complex 1 by RAD001 may induce upstream AKT upregulation. We hypothesized that dual inhibition of AKT along with mTOR will overcome the limited activity of RAD001 alone. METHODS: The BON cell line has been used as a model to study pancreatic neuroendocrine tumor cell biology. Western blots and cell growth assays were performed with mTOR inhibitor RAD001 (50 nM), mitogen-activated protein kinase inhibitor PD0325901 (50 nM), PI3K (phosphatidylinositol 3-kinase) inhibitor LY294002 (25 muM), or vehicle control. Nude mice were treated daily for 6 weeks with RAD001 (oral gavage) and with LY29400 (subcutaneous) 1 week after intrasplenic injection of BON cells. RESULTS: Cellular proliferation was most attenuated with the combination therapy of LY29400 and RAD001. Similarly, the volume of liver metastasis was lowest in the group treated with both LY29400 (100 mg/kg per week, subcutaneous) and RAD001 (2.5 mg/kg per day) compared with that in the vehicle group (P = 0.04). CONCLUSION: The combination therapy of LY29400 and RAD001 decreased the cell growth in vitro and progression of liver metastasis in vivo compared with vehicle or with single-drug therapy.

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[188]
TÍTULO / TITLE: - Arginase-1: A Highly Specific Marker Separating Pancreatic Adenocarcinoma from Hepatocellular Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Acta Cytol. 2013 Nov 20.
●● Enlace al texto completo (gratuito o de pago) 1159/000355629
AUTORES / AUTHORS: - Fatima N; Cohen C; Siddiqui MT
INSTITUCIÓN / INSTITUTION: - Department of Pathology and Laboratory Medicine, Emory University Hospital, Atlanta, Ga., USA.
RESUMEN / SUMMARY: - Background: Arginase-1 and HepPar-1 are effective immunohistochemical (IHC) markers for hepatocellular carcinoma (HCC). In this study, we explored the possible efficacy of these stains in diagnosing pancreatic adenocarcinoma (PAD). Study Design: Arginase-1 and HepPar-1 IHC was performed on formalin-fixed, paraffin-embedded fine needle aspiration (FNA) cell blocks (CB) of PAD (n = 46), tissue microarray (TMA) of PAD (n = 33), FNA CB of HCC (n = 44) and TMA of HCC (n = 85). Negative controls without carcinoma were also applied (pancreas CB, n = 7; pancreas TMA, n = 3). Results: PAD CB demonstrated arginase-1 positivity in 0 of 46 cases and HepPar-1 positivity in 7 of 46 cases (15%). PAD TMA demonstrated arginase-1 positivity in 0 of 33 cases and HepPar-1 positivity in 4 of 33

cases (12%). HCC CB demonstrated arginase-1 positivity in 37 of 44 cases (84%) and HepPar-1 positivity in 32 of 44 cases (72%). HCC TMA demonstrated arginase-1 positivity in 75 of 85 cases (88%) and HepPar-1 positivity in 80 of 85 cases (94%). Conclusion: Both arginase-1 and HepPar-1 are effective IHC markers of hepatocellular differentiation. Arginase-1 demonstrates superior sensitivity and specificity compared with HepPar-1 in the diagnosis of HCC. However, both arginase-1 and HepPar-1 have a low sensitivity and a very high specificity for PAD. © 2013 S. Karger AG, Basel.

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[189]

TÍTULO / TITLE: - Role of Radical Antegrade Modular Pancreatosplenectomy for Adenocarcinoma of the Body and Tail of the Pancreas.

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

REVISTA / JOURNAL: - World J Surg. 2013 Oct 29.

●● Enlace al texto completo (gratuito o de pago) 1007/s00268-013-2254-8

AUTORES / AUTHORS: - Park HJ; Do You D; Choi DW; Heo JS; Choi SH

INSTITUCIÓN / INSTITUTION: - Hepatobiliary Service, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul, 135-710, Korea, kipling22c@naver.com.

RESUMEN / SUMMARY: - BACKGROUND: Studies have claimed that in the surgical treatment of pancreas body and tail cancer, radical antegrade modular pancreatosplenectomy (RAMPS) is associated with effective tangential margin and extensive lymph node dissection. In the present study, the authors have compared the surgical outcomes between RAMPS and conventional distal pancreatosplenectomy (DPS) in patients with adenocarcinoma of the pancreas body and tail, and also identified prognostic factors associated with survival after surgery. METHODS: Retrospective review of 92 consecutive patients who underwent surgical resection for pancreas body and tail adenocarcinoma with curative intent between 1995 and 2010. Median follow-up duration was 16.1 months. RESULTS: Of the 92 patients, 38 patients received RAMPS and 54 patients received DPS. Patients who underwent RAMPS had a greater number of retrieved lymph nodes than patients undergoing DPS [median 14 (5-52) vs. 9 (1-36), $p < 0.05$]. Conventional DPS, no adjuvant chemoradiation therapy (CRT), and non-curative resection were associated with poor overall survival (OS) on univariate analysis. After multivariate analysis for these variables, only the lack of adjuvant CRT and resection margin status were found to adversely affect OS. CONCLUSIONS: While the RAMPS procedure is effective in performing an extensive LN dissection, it is not associated with better retroperitoneal resection margin or retrieval of more positive LNs, and it does not lead to better curability or OS survival compared to DPS. Lack of adjuvant CRT and resection margin status are poor prognostic factors in patients with pancreas body and tail cancer.

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[190]

TÍTULO / TITLE: - Modified FOLFIRINOX Regimen With Improved Safety and Maintained Efficacy in Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - Pancreas. 2013 Nov;42(8):1311-5. doi: 10.1097/MPA.0b013e31829e2006.

●● Enlace al texto completo (gratuito o de pago)
1097/MPA.0b013e31829e2006
AUTORES / AUTHORS: - Mahaseth H; Brutcher E; Kauh J; Hawk N; Kim S; Chen Z; Kooby DA; Maithel SK; Landry J; El-Rayes BF
INSTITUCIÓN / INSTITUTION: - From the *Department of Hematology and Medical Oncology, daggerBiostatistics and Bioinformatics Shared Resource at Winship Cancer Institute, double daggerDepartment of Biostatistics, section signDivision of Surgical Oncology, Department of Surgery, and parallelDepartment of Radiation Oncology, Emory University, Atlanta, GA.
RESUMEN / SUMMARY: - OBJECTIVES: FOLFIRINOX (5-fluorouracil [5-FU], oxaliplatin, and irinotecan) as compared with gemcitabine in pancreatic cancer (PC) has superior activity and increased toxicity. The bolus 5-FU contributes to the toxicity. We hypothesized that the elimination of bolus 5-FU and use of hematopoietic growth factor will improve the safety profile without compromising the activity of FOLFIRINOX. METHODS: Sixty patients with PC treated with modified FOLFIRINOX (no bolus 5-FU) were reviewed. Patients were divided into metastatic or nonmetastatic (locally advanced or borderline resectable) disease. Toxicity, response rate, progression-free survival, and overall survival were evaluated. RESULTS: Nonmetastatic and metastatic disease were present in 24 (40%) and 36 (60%) patients, respectively. The incidence of grade 4 neutropenia, grade ¾ diarrhea, and fatigue were 3%, 13%, and 13%, respectively. Response rate was 30%. The median progression-free survival for nonmetastatic disease was 13.7 months (95% confidence interval [CI], 9.6-24.6 months), and that for metastatic disease was 8.5 months (95% CI, 3.7-11.0 months), respectively. The median overall survival for nonmetastatic disease was 17.8 months (95% CI, 9.9 months to not estimable), and that for metastatic disease was and 9.0 months (95% CI, 7.1 months to not estimable), respectively. CONCLUSIONS: Modified FOLFIRINOX has an improved safety profile with maintained efficacy in metastatic PC. Modified FOLFIRINOX has promising activity in nonmetastatic disease.

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[191]
TÍTULO / TITLE: - Diabetes mellitus and pancreatic cancer: why the association matters?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreas. 2013 Nov;42(8):1207-9. doi: 10.1097/MPA.0b013e3182a7c963.
●● Enlace al texto completo (gratuito o de pago)
1097/MPA.0b013e3182a7c963
AUTORES / AUTHORS: - Hart PA; Chari ST
INSTITUCIÓN / INSTITUTION: - From the Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.

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[192]
TÍTULO / TITLE: - Pancreatic complications in pediatric choledochal cysts.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Pediatr Surg. 2013 Sep;48(9):1897-902. doi: 10.1016/j.jpedsurg.2012.12.038.

●● Enlace al texto completo (gratuito o de pago) 1016/j.jpedsurg.2012.12.038

AUTORES / AUTHORS: - Fujishiro J; Masumoto K; Urita Y; Shinkai T; Gotoh C

INSTITUCIÓN / INSTITUTION: - Department of Pediatric Surgery, Faculty of Medicine, University of Tsukuba, Japan. Electronic address: jfujishi-tky@umin.ac.jp.

RESUMEN / SUMMARY: - BACKGROUND/PURPOSE: The aim of this study is to clarify the clinical features and risk factors of pre- and postoperative pancreatic complications in pediatric choledochal cysts. METHODS: A retrospective chart review was carried out on pediatric patients with choledochal cysts who underwent radical operation at our department. RESULTS: Twenty-one, 24, and 24 patients were classified into the Todani Ia, Ic, and IV-A choledochal cyst, respectively. Preoperative acute pancreatitis and protein plugs were observed in 31 (43.7%) and 11 (15.5%) patients, respectively. Patients with preoperative pancreatitis were more likely to have fusiform dilatation of choledochal cysts (79.3% vs. 35.0%) and a dilated common channel (53.9% vs. 23.1%) compared to those without preoperative pancreatitis. Compared to patients without preoperative protein plugs, those with protein plugs were more likely to have fusiform dilatation (90.9% vs. 46.5%) and pancreatic divisum with communicating ducts and a dilated ductal system (60.0% vs. 2.5%). Postoperatively, three patients (4.2%) experienced acute pancreatitis. One of these and all 3 had protein plugs and preoperative pancreatitis, respectively. CONCLUSIONS: Fusiform-type choledochal cyst is a significant risk factor for preoperative pancreatic complications in choledochal cysts. While postoperative pancreatic complications were relatively rare, preoperative pancreatic complications might be risk factors for postoperative pancreatitis.

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[193]

TÍTULO / TITLE: - Pancreatitis-Diabetes-Pancreatic Cancer: Summary of an NIDDK-NCI Workshop.

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

REVISTA / JOURNAL: - Pancreas. 2013 Nov;42(8):1227-37. doi: 10.1097/MPA.0b013e3182a9ad9d.

●● Enlace al texto completo (gratuito o de pago) 1097/MPA.0b013e3182a9ad9d

AUTORES / AUTHORS: - Andersen DK; Andren-Sandberg A; Duell EJ; Goggins M; Korc M; Petersen GM; Smith JP; Whitcomb DC

INSTITUCIÓN / INSTITUTION: - From the *Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD; daggerDepartment of Surgery, Karolinska Institute, Stockholm, Sweden; double daggerUnit of Nutrition, Environment and Cancer, Catalan Institute of Oncology, Barcelona, España; section signDepartments of Medicine and Pathology, Johns Hopkins University School of Medicine, Baltimore, MD; parallelDepartments of Medicine and Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, IN; paragraph signDepartment of Epidemiology, Mayo Graduate School of Medicine, Rochester, MN; and #Departments of Medicine, Cell Biology and Physiology, and Human Genetics, University of Pittsburgh School of Medicine, Pittsburgh, PA.

RESUMEN / SUMMARY: - A workshop sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Cancer Institute (NCI) on “Pancreatitis-Diabetes-Pancreatic Cancer” focused on the risk factors of chronic

pancreatitis (CP) and diabetes mellitus (DM) on the development of pancreatic ductal adenocarcinoma (PDAC). Sessions were held on (a) an overview of the problem of PDAC; (b) CP as a risk factor of PDAC; (c) DM as a risk factor of PDAC; (d) pancreatogenic, or type 3c, DM; (e) genomic associations of CP, DM, and PDAC; (f) surveillance of high-risk populations and early detection of PDAC; and (g) effects of DM treatment on PDAC. Recent data and current understandings of the mechanisms of CP- and DM-associated factors on PDAC development were discussed, and a detailed review of the possible risks of DM treatment on the development of PDAC was provided by representatives from academia, industry, and the Food and Drug Administration. The current status of possible biomarkers of PDAC and surveillance strategies for high-risk populations were discussed, and the gaps in knowledge and opportunities for further research were elucidated. A broad spectrum of expertise of the speakers and the discussants provided an unusually productive workshop, the highlights of which are summarized in the accompanying article.

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[194]

TÍTULO / TITLE: - Pancreatic Cancer: Modulation of KRAS, MicroRNAs, and Intercellular Communication in the Setting of Tumor Heterogeneity.

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

REVISTA / JOURNAL: - Pancreas. 2013 Nov;42(8):1218-26. doi: 10.1097/MPA.0000000000000007.

●● Enlace al texto completo (gratuito o de pago)

1097/MPA.0000000000000007

AUTORES / AUTHORS: - Lou E; Subramanian S; Steer CJ

INSTITUCIÓN / INSTITUTION: - From the *Division of Hematology, Oncology and Transplantation, Departmentof Medicine; daggerDepartment of Surgery; and double daggerDivision of Gastroenterology, Hepatology and Nutrition, Department of Medicine, University of Minnesota, Minneapolis, MN.

RESUMEN / SUMMARY: - Supplemental digital content is available in the text. ABSTRACT: Mutations in KRAS-one of the ras family of oncogenes, encoding a GTPase critical to intracellular signal transduction-are more prevalent (80%-95%) in pancreatic cancer than in any other malignancy. There is increasing evidence that stromal cells-including pancreatic stellate cells-play a vital role in development and progression of pancreatic carcinomas. Advances in understanding the underlying biology of tumor-stroma interactions and tumor heterogeneity are critical to guiding rational approaches to designing treatments tailored to targeting KRAS in the stroma-rich microenvironment. Areas of interest in creating novel approaches to therapy include elucidating interactions of KRAS with microRNAs, the role of intratumoral hypoxia, and exploration of diverse modes of intercellular propagation of signals that stimulate malignant invasion and metastasis. This article provides an overview and state-of-the-art update of knowledge regarding pancreatic tumor biology, with a special focus on pancreatic tumor heterogeneity, the role of microRNA-mediated and hypoxic alterations in gene expression and interactions with KRAS, intercellular communication and trafficking, and progress in understanding KRAS as a potential target for pancreatic cancer therapy.

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[195]
TÍTULO / TITLE: - Mutational analysis of cytocentrifugation supernatant fluid from pancreatic solid mass lesions.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Diagn Cytopathol. 2013 Nov 22. doi: 10.1002/dc.23048.
●● Enlace al texto completo (gratuito o de pago) 1002/dc.23048
AUTORES / AUTHORS: - Finkelstein SD; Bibbo M; Kowalski TE; Loren DE; Siddiqui AA; Solomides C; Ellsworth E
INSTITUCIÓN / INSTITUTION: - RedPath Integrated Pathology, Inc., Pittsburgh, Pennsylvania, USA.
RESUMEN / SUMMARY: - Diagnosis of fine-needle aspirations of pancreatic solid masses is complicated by many factors that keep its false-negative rate high. Our novel approach analyzes cell-free cytocentrifugation supernatant, currently a discarded portion of the specimen. Supernatant and cytology slides were collected from 25 patients: 11 cases with confirmed outcome [five positive (adenocarcinoma) and six negative (inflammatory states)], plus 14 without confirmed outcomes. Slides were microdissected, DNA was extracted from microdissections and corresponding supernatants, and all were analyzed for KRAS point mutation and loss of heterozygosity. Notably, higher levels of free DNA were found in supernatants than in corresponding microdissected cells. Supernatants contained sufficient DNA for mutational profiling even when samples contained few to no cells. Mutations were present in 5/5 malignancies and no mutations were present in inflammatory states. In conclusion, these findings support using supernatant for mutational genotyping when diagnostic confirmation is required for pancreatic solid masses. Diagn. Cytopathol. 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.

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[196]
TÍTULO / TITLE: - Favorable response after gemcitabine-radiotherapy for invasive pancreatic intraductal papillary mucinous neoplasm: a case report.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Int Surg. 2013 Oct-Dec;98(4):340-5. doi: 10.9738/INTSURG-D-13-00031.1.
●● Enlace al texto completo (gratuito o de pago) 9738/INTSURG-D-13-00031.1
AUTORES / AUTHORS: - Ochiai T; Igari K; Furuyama T; Ito H; Mitsunori Y; Aihara A; Kumagai Y; Iida M; Odajima H; Tanaka S; Arii S; Yamazaki S
INSTITUCIÓN / INSTITUTION: - 1 Department of Hepato-Biliary-Pancreatic Surgery, Graduate School of Medicine, Tokyo Medical and Dental University, Tokyo, Japan.
RESUMEN / SUMMARY: - Abstract The efficacy of chemoradiotherapy for invasive pancreatic ductal carcinoma derived from an intraductal papillary mucinous neoplasm

(IPMN) has not been established. The subject of the present report was a 53-year-old man admitted for the treatment of IPMN. The tumor, located in the pancreatic body, was of the mixed type of IPMN, and it involved the branch duct, where it was 38 mm in diameter, and the main duct, where it was 6 mm in diameter. Distal pancreatectomy was performed and the postoperative course was uneventful; however, histopathologic diagnosis revealed invasive ductal carcinoma with a positive surgical margin in the pancreatic duct. Although total pancreatectomy was recommended, chemoradiotherapy (50.4-Gy irradiation and gemcitabine) was preferred by the patient. At 9-month follow up, computed tomography and magnetic resonance imaging showed a cystic mass at the surgical margin of the pancreas. Endoscopic ultrasonography showed a 44-mm cystic lesion with nodules in the remnant pancreas, on the basis of which he underwent total pancreatectomy. Pathologic examination of the resected specimen revealed absence of the epithelium at the surgical margin of the main pancreatic duct, and malignant cells were not detected.

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[197]

TÍTULO / TITLE: - Syndrome of Inappropriate Secretion of Antidiuretic Hormone due to Selective Serotonin Reuptake Inhibitors After Pancreaticoduodenectomy for Carcinoma of the Ampulla of Vater: Case Report.

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

REVISTA / JOURNAL: - Int Surg. 2013 Oct-Dec;98(4):289-91. doi: 10.9738/INTSURG-D-13-00032.1.

●● Enlace al texto completo (gratuito o de pago) 9738/INTSURG-D-13-00032.1

AUTORES / AUTHORS: - Iwase R; Shiba H; Gocho T; Futagawa Y; Wakiyama S; Ishida Y; Misawa T; Yanaga K

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The Jikei University School of Medicine, Tokyo, Japan.

RESUMEN / SUMMARY: - Abstract A 68-year-old man underwent pancreaticoduodenectomy with lymph nodes dissection for carcinoma of the ampulla of Vater. The patient had anxiety neurosis and had been treated with a selective serotonin reuptake inhibitor (SSRI). Postoperatively, SSRI was resumed on postoperative day 2. His serum sodium concentration gradually decreased, and the patient was given a sodium supplement. However, 11 days after the operation, laboratory findings included serum sodium concentration of 117 mEq/L, serum vasopressin of 2.0 pg/mL, plasma osmolality of 238 mOsm/kg, urine osmolality of 645 mOsm/kg, urine sodium concentration of 66 mEq/L, serum creatinine concentration of 0.54 mg/dL, and serum cortisol concentration of 29.1 mug/dL. With a diagnosis of syndrome of inappropriate secretion of antidiuretic hormone (SIADH), the antianxiety neurosis medication was changed from the SSRI to another type of drug. After switching the medication, the patient made a satisfactory recovery with normalization of serum sodium by postoperative day 20.

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[198]

TÍTULO / TITLE: - Gastric conduit-preserving, radical pancreaticoduodenectomy with microvascular reconstruction for pancreatic head cancer after esophagectomy: report of a case.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Surg Today. 2013 Nov 22.
●● Enlace al texto completo (gratuito o de pago) 1007/s00595-013-0791-2
AUTORES / AUTHORS: - Inoue A; Akita H; Eguchi H; Hama N; Wada H; Kawamoto K; Kobayashi S; Mori M; Doki Y; Nagano H
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Yamadaoka 2-2(E2), Suita, Osaka, 565-0871, Japan.
RESUMEN / SUMMARY: - Pancreaticoduodenectomy is a radical treatment for pancreatic head cancer. However, it is sometimes difficult to perform pancreaticoduodenectomy, particularly in patients who have previously undergone esophagectomy with gastric conduit reconstruction. We herein describe a surgical technique for radical pancreaticoduodenectomy with microvascular reconstruction that preserves the gastric conduit. A 72-year-old male with a previous history of esophagectomy and gastric conduit reconstruction for esophageal cancer was referred to our hospital for surgical treatment of advanced pancreatic head cancer. After considering both the cancer curability and preservation of the gastric conduit, we performed a standard pancreaticoduodenectomy, and added a microvascular anastomosis of the gastroduodenal artery to the right gastroepiploic artery. In addition, we also performed reconstruction of the right gastroepiploic vein. This radical pancreaticoduodenectomy with microvascular reconstruction was safely and successfully performed, and it preserved the gastric conduit. The 6-month follow-up showed recurrence-free survival and a good quality of life.

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[199]
TÍTULO / TITLE: - Molecular diagnostics in the neoplasms of the pancreas, liver, gall bladder, and extrahepatic biliary tract.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Lab Med. 2013 Dec;33(4):875-80. doi: 10.1016/j.cll.2013.08.002. Epub 2013 Oct 9.
●● Enlace al texto completo (gratuito o de pago) 1016/j.cll.2013.08.002
AUTORES / AUTHORS: - Weindel M; Zulfiqar M; Bhalla A; Shidham VB
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Detroit Medical Center, Karmanos Cancer Center, Wayne State University School of Medicine, 540 East Canfield, Detroit, MI 48201, USA.
RESUMEN / SUMMARY: - Pancreatic neoplasms, including ductal adenocarcinoma, intraductal papillary mucinous neoplasm, solid pseudopapillary neoplasm, pancreatic endocrine neoplasms, acinar cell carcinoma, and ampullary carcinoma, are associated with different genetic abnormalities. Liver neoplasms, including hepatic adenomas, hepatocellular carcinomas, and cholangiocarcinomas, are associated with identifiable risk factors and genetic changes. Gall bladder adenomas and adenocarcinomas arise from distinct molecular pathways. The molecular abnormalities seen in these tumors are not used routinely in the molecular diagnostic laboratory.

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[200]

TÍTULO / TITLE: - Delineating the effects BRCA1 and BRCA2 loss of heterozygosity in pancreatic cancer progression.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Genet. 2013 Oct 21. doi: 10.1111/cge.12306.
●● Enlace al texto completo (gratuito o de pago) 1111/cge.12306
AUTORES / AUTHORS: - Fam H
INSTITUCIÓN / INSTITUTION: - Department of Medical Genetics, University of British Columbia, 950 West 28th Avenue, Vancouver, British Columbia, V5Z4H4, Canada. hfam@cfri.ca.
RESUMEN / SUMMARY: - High prevalence of BRCA1 and BRCA2 germline mutations with loss of heterozygosity in a series of resected pancreatic adenocarcinoma and other neoplastic lesions Lucas et al. (2013) Clinical Cancer Research 19(13): 3396-3403.

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[201]
TÍTULO / TITLE: - Dual Tracer Functional Imaging of Gastroenteropancreatic Neuroendocrine Tumors Using 68Ga-DOTA-NOC PET-CT and 18F-FDG PET-CT: Competitive or Complimentary?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Nucl Med. 2013 Nov 7.
●● Enlace al texto completo (gratuito o de pago)
1097/RLU.0b013e31827a216b
AUTORES / AUTHORS: - Naswa N; Sharma P; Gupta SK; Karunanithi S; Reddy RM; Patnecha M; Lata S; Kumar R; Malhotra A; Bal C
INSTITUCIÓN / INSTITUTION: - From the Department of Nuclear Medicine, All India Institute of Medical Sciences, New Delhi, India.
RESUMEN / SUMMARY: - OBJECTIVE: This study aimed to compare the diagnostic performance of Ga-DOTANOC PET/CT with F-FDG PET/CT in the patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs). PATIENTS AND METHODS: Data of 51 patients with definite histological diagnosis of GEP-NET who underwent both Ga-DOTA-NOC PET-CT and F-FDG PET-CT within a span of 15 days were selected for this retrospective analysis. Sensitivity, specificity, and predictive values were calculated for Ga-DOTA-NOC PET-CT and F-FDG PET-CT, and results were compared both on patientwise and regionwise analysis. RESULTS: Ga-DOTA-NOC PET-CT is superior to F-FDG PET-CT on patientwise analysis ($P < 0.0001$). On regionwise analysis, Ga-DOTA-NOC PET-CT is superior to F-FDG PET-CT only for lymph node metastases ($P < 0.003$). Although Ga-DOTA-NOC PET-CT detected more liver and skeletal lesions compared with F-FDG PET-CT, the difference was not statistically significant. In addition, the results of combined imaging helped in selecting candidates who would undergo the appropriate mode of treatment, whether octreotide therapy or conventional chemotherapy CONCLUSIONS: Ga-DOTA-NOC PET-CT seems to be superior to F-FDG PET-CT for imaging GEP-NETs. However, their role seems to be complementary because combination of Ga-DOTA-NOC PET-CT and F-FDG PET-CT in such patients helps demonstrate the total disease burden and segregate them to proper therapeutic groups.

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[202]
TÍTULO / TITLE: - Advances of high intensity focused ultrasound (HIFU) for pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Int J Hyperthermia. 2013 Nov;29(7):678-82. doi: 10.3109/02656736.2013.837199.
●● Enlace al texto completo (gratuito o de pago) 3109/02656736.2013.837199
AUTORES / AUTHORS: - Xiaoping L; Leizhen Z
INSTITUCIÓN / INSTITUTION: - Department of Oncology, Xinhua Hospital, Shanghai Jiaotong University , Shanghai 200092 , China.
RESUMEN / SUMMARY: - High intensity focused ultrasound (HIFU) is a novel therapeutic modality. Several preclinical and clinical studies have investigated the safety and efficacy of HIFU for treating solid tumours, including pancreatic cancer. Preliminary studies suggest that HIFU may be useful for the palliative therapy of cancer-related pain in patients with unresectable pancreatic cancer. This review provides a brief overview of HIFU, describes current clinical applications of HIFU for pancreatic cancer, and discusses future applications and challenges.

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[203]
TÍTULO / TITLE: - Hepatobiliary and Pancreatic: Large pancreatic liposarcoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Gastroenterol Hepatol. 2013 Dec;28(12):1800. doi: 10.1111/jgh.12433.
●● Enlace al texto completo (gratuito o de pago) 1111/jgh.12433
AUTORES / AUTHORS: - Kuramoto K; Hashimoto D; Abe S; Chikamoto A; Beppu T; Iyama K; Baba H
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery, Kumamoto University Graduate School of Medical Sciences, Kumamoto, Japan.

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[204]
TÍTULO / TITLE: - Standard Retrograde Pancreatosplenectomy versus Radical Antegrade Modular Pancreatosplenectomy for Body and Tail Pancreatic Adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Am Surg. 2013 Nov;79(11):1154-8.
AUTORES / AUTHORS: - Latorre M; Ziparo V; Nigri G; Balducci G; Cavallini M; Ramacciato G
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Surgical Department of Clinical Sciences, Biomedical Technologies and Translational Medicine, Faculty of Medicine and Psychology, University of Rome “La Sapienza,” St. Andrea Hospital, Rome, Italy.
RESUMEN / SUMMARY: - Pancreatic surgery remains the only established curative treatment for pancreatic cancer. Radical antegrade pancreatosplenectomy (RAMPS) is a modification of the standard retrograde pancreatosplenectomy (SRPS) developed to achieve a complete N1 node resection and R0 resection (posterior extent). The aim of this study is to compare the short-, mid-, and long-term outcomes of RAMPS and

SRPS. From a database that included 143 consecutive patients who underwent resection for pancreatic carcinoma at the St. Andrea Hospital, University of Rome, 25 patients who underwent pancreatosplenectomy were retrospectively reviewed. Among these 25 patients, eight (32%) underwent RAMPS (Group 1) and 17 (68%) underwent SRPS (Group 2). Clinicopathologic and oncological characteristics of the RAMPS group were compared with those of the SRPS group. RAMPS was longer than SRPS (315 vs 265 minutes, respectively, P < 0.001). No differences were encountered for perioperative outcomes (estimated blood loss, intraoperative blood transfusions, postoperative morbidity and mortality, and hospital stay). The margin status rates were similar: noteworthy, the two patients with positive tangential margins belonged to Group 2. No between-group differences in survival were encountered: the actuarial 5-year overall survival for Groups 1 and 2 were 26 and 29 per cent, respectively (P = 0.6608; hazard ratio, 1.2621; 95% confidence interval, 0.4462 to 3.5699). RAMPS and SRPS did not differ statistically in terms of perioperative outcomes. RAMPS seems to allow better control of tangential margins; however, no difference was found in actuarial survival compared with standard pancreatosplenectomy.

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[205]

TÍTULO / TITLE: - Management of pancreatic fistulas after a splenectomy as part of cytoreductive surgery for ovarian cancer.

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

REVISTA / JOURNAL: - Int J Gynecol Cancer. 2013 Oct;23(8):1506-11. doi: 10.1097/IGC.0b013e3182a0fa66.

●● Enlace al texto completo (gratuito o de pago) 1097/IGC.0b013e3182a0fa66

AUTORES / AUTHORS: - Kato K; Tate S; Nishikimi K; Shozu M

INSTITUCIÓN / INSTITUTION: - Department of Gynecology, Chiba University School of Medicine, Chuo-ku, Chiba, Japan.

RESUMEN / SUMMARY: - OBJECTIVE: This study evaluated the incidence of postoperative morbidities, focusing specifically on pancreatic fistulas, after a splenectomy performed as part of cytoreductive surgery for the treatment of ovarian cancer. METHODS: A retrospective chart review was performed for all the patients with ovarian, tubal, or peritoneal cancer who underwent splenectomy during a 5-year period. Patient-, disease-, and surgery-related data were collected. Pancreatic fistulas were identified when the drainage fluid obtained via a surgically placed drain had an amylase content greater than 3 times the normal serum value after postoperative day 3. RESULTS: A splenectomy was performed in 21 patients. Postoperative pancreatic fistulas developed in 6 patients (29%). Of these 6 patients, 2 had no symptoms and did not require specific treatment for their pancreatic fistulas. Therapeutic intervention was required in the remaining 4 patients. The durations of oral feeding prohibition and the use of a peripancreatic drain were longer in the patients with a pancreatic fistula than in those without a pancreatic fistula. Overall, the pancreatic fistulas were managed conservatively or using minimally invasive procedures. Staple-line reinforcement seemed to be an effective means of closing the transected stump during the splenectomy, compared with the standard stapling technique. CONCLUSIONS: Elevated amylase levels in the drainage fluid reflect the patient's actual condition better than serum amylase levels. We recommend the intraoperative placement of a peripancreatic drain and postoperative measurement of amylase concentrations in the

drainage fluid to identify the development of pancreatic fistulas and to facilitate the management of this complication.

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[206]

TÍTULO / TITLE: - Quantified ADC histogram analysis: a new method for differentiating mass-forming focal pancreatitis from pancreatic cancer.

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

REVISTA / JOURNAL: - Acta Radiol. 2013 Oct 28.

●● Enlace al texto completo (gratuito o de pago) 1177/0284185113509264

AUTORES / AUTHORS: - Ma X; Zhao X; Ouyang H; Sun F; Zhang H; Zhou C

INSTITUCIÓN / INSTITUTION: - Diagnostic Radiology, Cancer Hospital, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, People's Republic of China.

RESUMEN / SUMMARY: - BACKGROUND: As their prognosis and management are different, differentiation of mass-forming focal pancreatitis (FP) from pancreatic adenocarcinoma (PC) is important. However, the similar clinical presentations and imaging features of these conditions, along with inconclusive biopsy results can make such differentiation difficult. PURPOSE: To determine whether apparent diffusion coefficient (ADC) histogram analysis can discriminate between a normal pancreas, FP, and PC. MATERIAL AND METHODS: In a retrospective study, 25 PC patients, 14 FP patients, and 25 subjects with a normal pancreas underwent breath-hold diffusion-weighted imaging (DWI) on a 3.0 T magnetic resonance (MR) scanner. Regions of interest (ROIs) were drawn on the normal pancreases and on the entire focal lesions of both PC and FP. The ADC value was averaged from the lowest to 10^{th}, 30^{th}, 50^{th}, and 100^{th} percentile of the histogram (i.e. ADC10, ADC30, ADC50, and ADC100, respectively), and the results were analyzed statistically. RESULTS: There were no significant differences among the head, body, and tail of normal pancreases for any of the mean ADC values ($P > 0.05$). ADC10, ADC30, and ADC50 values demonstrated significant differences between lesion and non-lesion areas of both PC ($P < 0.05$) and FP ($P < 0.05$). Differences in lesion areas between PC and FP were found with ADC50 and ADC100 values ($P < 0.05$), and helped differentiate a normal pancreas from FP and PC, and FP from PC. CONCLUSION: Quantified ADC histogram can specifically reflect tissue heterogeneity and help differentiate a normal pancreas from FP and PC.

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[207]

TÍTULO / TITLE: - Gastroenteropancreatic neuroendocrine neoplasms: historical context and current issues.

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

REVISTA / JOURNAL: - Semin Diagn Pathol. 2013 Aug;30(3):186-96. doi: 10.1053/j.semdp.2013.06.005.

●● Enlace al texto completo (gratuito o de pago) 1053/j.semdp.2013.06.005

AUTORES / AUTHORS: - Yang Z; Tang LH; Klimstra DS

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania.

RESUMEN / SUMMARY: - The digestive organs contain a large number of neuroendocrine cells as part of the diffuse neuroendocrine system. Neuroendocrine

tumors can occur in every digestive organ. It has long been recognized that this is a diverse group of tumors with very different clinical outcomes; however, well-recognized prognostic parameters had been elusive until recently. Over the years, there have been several different classification schemes, each with different strengths and weaknesses. In an effort to standardize the classification and grading criteria for gastroenteropancreatic neuroendocrine tumors, the current World Health Organization classification includes a histologic grade based on proliferative rate (mitotic rate and Ki67 index) and a TNM stage that varies from organ to organ. The prognostic value of both the grade and stage has been validated in multiple studies. However, several issues remain, including the lack of standardized methods to assess proliferative rate, potential discrepancies between the mitotic count and the Ki67 index; intratumoral heterogeneity in proliferative rate; and the need for refinement in proliferative cut-points to define the grades. More studies are needed to further improve the classification of neuroendocrine tumors, thus guiding optimal treatment for these tumors.

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[208]

TÍTULO / TITLE: - Significance of atypia in pancreatic and bile duct brushings: Follow-Up analysis of the categories atypical and suspicious for malignancy.

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

REVISTA / JOURNAL: - Diagn Cytopathol. 2013 Oct 25. doi: 10.1002/dc.23035.

●● Enlace al texto completo (gratuito o de pago) 1002/dc.23035

AUTORES / AUTHORS: - Chadwick BE; Layfield LJ; Witt BL; Schmidt RL; Cox RN; Adler DG

INSTITUCIÓN / INSTITUTION: - Department of Pathology, University of Utah School of Medicine and ARUP Laboratories, Salt Lake City, Utah.

RESUMEN / SUMMARY: - Brushing cytology is frequently utilized for the investigation of pancreatic and biliary strictures but is associated with low diagnostic sensitivity. The Papanicolaou Society of Cytopathology has presented a system for diagnostic classification which includes the categories benign, atypical, suspicious for malignancy and malignant. We studied a series of 216 pancreatic and biliary brushings with either histologic follow-up or a minimum of 6 months clinical follow-up to determine outcomes for the diagnostic categories (“benign,” “atypical, favor reactive,” “atypical, not otherwise specified,” “atypical, suspicious” and “malignant”). Eighty-six of the 216 (39.8%) were designated “atypical” with 10 of these designated as “atypical favor reactive.” Forty-five were called “atypical not otherwise specified” and 31 were interpreted as “atypical suspicious for malignancy.” On follow-up, 2 of 10 (20%) “atypical favor reactive” were eventually associated with a malignant diagnosis and 23 of 31 (74.2%) “atypical, suspicious for malignancy” demonstrated a malignant outcome. The remaining 45 brushings in the “atypical” category were “atypical not otherwise specified,” and 62% of these were associated with malignancy on follow-up. Stratification of the “atypical” category into “atypical favor reactive,” “atypical, not otherwise specified” and “atypical, suspicious for malignancy” improves diagnostic accuracy. The “atypical suspicious for malignancy” category has a follow-up similar to the “malignant” category while the “atypical favor reactive” category is associated with a clinical outcome similar to that of the “benign” category. Diagn. Cytopathol. © 2013 Wiley Periodicals, Inc.

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[209]

TÍTULO / TITLE: - Patterns of FDG uptake in pancreatic non-Hodgkin's lymphoma lesions.

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

REVISTA / JOURNAL: - Abdom Imaging. 2013 Oct 18.

●● Enlace al texto completo (gratuito o de pago) 1007/s00261-013-0041-5

AUTORES / AUTHORS: - Dong A; Cui Y; Gao L; Wang Y; Zuo C; Yang J

INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, Changhai Hospital, Second Military Medical University, 168 Changhai Road, Yangpu, Shanghai, 200433, China.

RESUMEN / SUMMARY: - Purpose: The aim of this study was to evaluate the pattern of FDG uptake in pancreatic non-Hodgkin's lymphoma (NHL) lesions. Methods: The study included 9 consecutive patients with newly diagnosed NHL with pancreatic involvement who underwent an F-18 fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) scan. The location, size, maximal standardized uptake value (SUVmax), and FDG uptake patterns of the pancreatic lesions were reviewed. Results: Four different patterns of FDG uptake could be distinguished in the affected pancreas corresponding to different types of lymphoma lesions. These included focal FDG uptake by distinct solitary lesions (5 patients), multiple foci of FDG uptake corresponding to separate lymphoma lesions (1 patient), segmental FDG uptake caused by lymphoma infiltration limited to a pancreatic segment (1 patient), and diffuse FDG uptake related to diffuse lymphomatous infiltration of the entire pancreas (2 patients). All types of lesions showed increased metabolic activity with maximal standardized uptake values (SUVmax) ranging from 7.4 to 26.5. On CT images, the segmental and diffuse patterns of FDG uptake correlated to segmental and diffuse pancreatic enlargement accordingly. All lesions showed isodensity or slight hypodensity in relation to pancreatic tissue. The pancreatic head was the most frequent site of involvement (8/9). Mildly dilated pancreatic duct was noted only in 2 patients. Conclusions: The described patterns of FDG uptake and correlative CT findings may be helpful for a better characterization of NHL involving the pancreas and for differential diagnosis with other lesions, including pancreatic adenocarcinomas.

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[210]

TÍTULO / TITLE: - Elevated Ki-67 labeling index in 'synchronous liver metastases' of well differentiated enteropancreatic neuroendocrine tumor.

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

REVISTA / JOURNAL: - Pathol Int. 2013 Nov;63(11):532-8. doi: 10.1111/pin.12108.

●● Enlace al texto completo (gratuito o de pago) 1111/pin.12108

AUTORES / AUTHORS: - Zen Y; Heaton N

INSTITUCIÓN / INSTITUTION: - Histopathology Section, King's College London School of Medicine at King's College Hospital, London, UK.

RESUMEN / SUMMARY: - There is no consensus as to whether or not metastatic nodules in the liver should be biopsied for tumor grading in cases of neuroendocrine tumors with 'synchronous liver metastasis'. In this study, we compared the Ki-67 labeling index between the primary tumor and synchronous liver metastasis in 30 patients, who had received simultaneous resections. Examined tumors were of the

small bowel (n = 18) or pancreas (n = 12), and G1 or G2 in primary histologic grade. In 20 patients (67%), the Ki-67 index was similar between the primary tumor and liver metastasis, but 10 (33%) showed an elevation of 3.4-14.4% in the liver, which increased the tumor grade in 4 cases. The Ki-67 elevation in the liver was more common in G2 than G1 neoplasms (P = 0.002). The size, but not number, of liver metastases was significantly larger in patients with an elevated Ki-67 index (P = 0.006). Using 40 mm as a provisional cutoff for the greatest diameter of liver metastases, the positive predictive value of this discriminator for elevated Ki-67 was 56%, and the negative predictive value was 93%. In conclusion, synchronous liver metastases can yield a higher Ki-67 labeling index than primary neuroendocrine tumours, particularly when the secondary is greater than 40 mm.

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[211]

TÍTULO / TITLE: - Laparoscopic vs open distal pancreatectomy for solid pseudopapillary tumor of the pancreas.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Oct 7;19(37):6272-7. doi: 10.3748/wjg.v19.i37.6272.

●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i37.6272

AUTORES / AUTHORS: - Zhang RC; Yan JF; Xu XW; Chen K; Ajoodhea H; Mou YP

INSTITUCIÓN / INSTITUTION: - Ren-Chao Zhang, Jia-Fei Yan, Xiao-Wu Xu, Ke Chen, Harsha Ajoodhea, Yi-Ping Mou, Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou 310016, Zhejiang Province, China.

RESUMEN / SUMMARY: - AIM: To compare short- and long-term outcomes of laparoscopic vs open distal pancreatectomy for solid pseudopapillary tumor (SPT) of the pancreas. METHODS: This retrospective study included 28 patients who underwent distal pancreatectomy for SPT of the pancreas between 1998 and 2012. The patients were divided into two groups based on the surgical approach: the laparoscopic surgery group and the open surgery group. The patients' demographic data, operative results, pathological reports, hospital courses, morbidity and mortality, and follow-up data were compared between the two groups. RESULTS: Fifteen patients with SPT of the pancreas underwent laparoscopic distal pancreatectomy (LDP), and 13 underwent open distal pancreatectomy (ODP). Baseline characteristics were similar between the two groups except for a female predominance in the LDP group (100.0% vs 69.2%, P = 0.035). Mortality, morbidity (33.3% vs 38.5%, P = 1.000), pancreatic fistula rates (26.7% vs 30.8%, P = 0.728), and reoperation rates (0.0% vs 7.7%, P = 0.464) were similar in the two groups. There were no significant differences in the operating time (171 min vs 178 min, P = 0.755) between the two groups. The intraoperative blood loss (149 mL vs 580 mL, P = 0.002), transfusion requirement (6.7% vs 46.2%, P = 0.029), first flatus time (1.9 d vs 3.5 d, P = 0.000), diet start time (2.3 d vs 4.9 d, P = 0.000), and postoperative hospital stay (8.1 d vs 12.8 d, P = 0.029) were significantly less in the LDP group than in the ODP group. All patients had negative surgical margins at final pathology. There were no significant differences in number of lymph nodes harvested (4.6 vs 6.4, P = 0.549) between the two groups. The median follow-up was 33 (3-100) mo for the LDP group and 45 (17-127) mo for the ODP group. All patients were alive with one recurrence. CONCLUSION: LDP for SPT

has short-term benefits compared with ODP. Long-term outcomes of LDP are similar to those of ODP.

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[212]
TÍTULO / TITLE: - Unusual early-stage pancreatic sarcomatoid carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - World J Gastroenterol. 2013 Nov 21;19(43):7820-4. doi: 10.3748/wjg.v19.i43.7820.
●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i43.7820
AUTORES / AUTHORS: - Ren CL; Jin P; Han CX; Xiao Q; Wang DR; Shi L; Wang DX; Chen H
INSTITUCIÓN / INSTITUTION: - Chuan-Li Ren, Ping Jin, Chong-Xu Han, Laboratory Medicine and Pathology Department, Northern Jiangsu People's Hospital and Clinical Medical College of Yangzhou University, Yangzhou 225001, Jiangsu Province, China.
RESUMEN / SUMMARY: - Sarcomatoid carcinoma of the pancreas (SCP) is a very rare pathological type of carcinoma that usually has a poor prognosis. Its pathogenesis has not been elucidated. We herein report a case of an early-stage SCP involving successful treatment and a good prognosis. The patient was a 48-year-old Chinese man with a 5-mo history of vague abdominal pain. Ultrasonography revealed a 93 mm x 94 mm x 75 mm mass of mixed echogenicity in the tail of the pancreas. Laboratory test results were within the normal range, with the exception of an obviously increased pretreatment neuron-specific enolase level. The plasma transforming growth factor (TGF)beta1 and interleukin-11 levels were obviously increased according to enzyme-linked immunosorbent assay. Microscopically, the excised tumor tissue comprised cancer cells and mesenchymal cells. Immunohistochemical analysis was positive for alpha-1-antichymotrypsin, pan-cytokeratin, cytokeratin 19, cytokeratin 8/18, and vimentin and negative for CD68 and lysozyme. The pathogenetic mechanism of this case shows that TGFbeta1 may regulate the epithelial-to-mesenchymal transition in SCP. With early eradication of the tumor and systemic therapy, this patient has been alive for more than 3 years without tumor recurrence or distant metastasis. This case is also the first to show that TGFbeta1 may regulate the epithelial-to-mesenchymal transition in early-stage SCP.

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[213]
TÍTULO / TITLE: - Pancreatic Hepatoid Carcinoma: A Review of the Literature.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Dig Surg. 2013 Nov 22;30(4-6):425-433.
●● Enlace al texto completo (gratuito o de pago) 1159/000355442
AUTORES / AUTHORS: - Marchegiani G; Gareer H; Parisi A; Capelli P; Bassi C; Salvia R
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Verona University Hospital, Verona, Italy.
RESUMEN / SUMMARY: - Background: Hepatoid carcinomas (HCs) are extrahepatic neoplasms exhibiting features of hepatocellular tumors in terms of morphology and immunohistochemistry. They have been described in several organs, most notably in the stomach and ovary. They can present in pure forms or in association with other

morphological aspects, such as endocrine tumors or ductal adenocarcinomas. The aim of this review is to describe aspects of hepatoid adenocarcinoma of the pancreas with regard to epidemiology, diagnosis, and treatment. Methods: The PubMed database was searched for publications addressing hepatoid adenocarcinoma of the pancreas. We have searched for articles including the following keywords: 'pancreatic hepatoid carcinoma', 'ectopic liver cancer' and 'rare pancreas neoplasm' published to date. As references, we used case reports and review articles. Results: Pancreatic forms of HCs are extremely uncommon: only 22 cases have been reported. Conclusions: The possibility of an HC of the pancreas should be considered in the differential diagnosis of an uncommon pathological mass of the pancreas. Treatment seems to be related to the association with other neoplasms, tumor extension at the time of diagnosis and the possibility to perform a radical resection. The common embryologic origin of the pancreas and liver, together with peculiar environmental factors, may explain the development of pancreatic HCs. © 2013 S. Karger AG, Basel.

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[214]

TÍTULO / TITLE: - Splenule Disguised as Pancreatic Mass: Elucidated With SPECT Liver-Spleen Scintigraphy.

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

REVISTA / JOURNAL: - Clin Nucl Med. 2013 Oct 3.

●● Enlace al texto completo (gratuito o de pago)

1097/RLU.0b013e3182a75829

AUTORES / AUTHORS: - Shah M; McClelland A; Moadel R; Javed AA; Freeman LM

INSTITUCIÓN / INSTITUTION: - From the *Division of Nuclear Medicine, Department of Radiology, Montefiore Medical Center and the Albert Einstein College of Medicine of Yeshiva University, Bronx, NY; and daggerWayne State University School of Medicine, Detroit, MI.

RESUMEN / SUMMARY: - Splenules are congenital foci of healthy splenic tissue that are separate from the main body but are structurally identical to the spleen, derived from mesenchymal buds on the left side of the mesogastrium and commonly seen in or near the tail of the pancreas. We report a case of a 58-year-old male who was found to have a pancreatic tail mass on contrast-enhanced abdominal CT, which was similarly disguised as a pancreatic tail mass on both magnetic resonance cholangiopancreatography and abdominal MRI. A liver spleen scintigraph with Tc sulfur colloid later proved the mass to be a splenule.

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[215]

TÍTULO / TITLE: - Improvement of surgical results for pancreatic cancer.

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

REVISTA / JOURNAL: - Lancet Oncol. 2013 Oct;14(11):e476-85. doi: 10.1016/S1470-2045(13)70172-4.

●● Enlace al texto completo (gratuito o de pago) 1016/S1470-2045(13)70172-4

AUTORES / AUTHORS: - Hartwig W; Werner J; Jager D; Debus J; Buchler MW

INSTITUCIÓN / INSTITUTION: - Department of General, Visceral, and Transplantation Surgery, University of Heidelberg, Heidelberg, Germany.

RESUMEN / SUMMARY: - Surgery is the only potential hope of cure for patients with pancreatic cancer. Advantageous tumour characteristics and complete tumour resection are the factors most relevant for a positive prognosis, so detection of premalignant or early invasive lesions, combined with safe and oncologically adequate surgery, is an important goal. The experience and volume of both the individual surgeon and hospital are of paramount importance to achieve low morbidity and adequate management of complications. Most pancreatic cancers are locally advanced or metastatic when diagnosed and need multimodal therapy. With increasing evidence on surgical and perioperative aspects of pancreatic cancer therapy, short-term and long-term outcomes of resectable and borderline resectable pancreatic cancer are improving.

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[216]

TÍTULO / TITLE: - Pancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - Curr Probl Surg. 2013 Nov;50(11):509-45. doi: 10.1067/j.cpsurg.2013.08.001.

●● Enlace al texto completo (gratuito o de pago) 1067/j.cpsurg.2013.08.001

AUTORES / AUTHORS: - Krampitz GW; Norton JA

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[217]

TÍTULO / TITLE: - Mapping PAM4 (clivatuzumab), a monoclonal antibody in clinical trials for early detection and therapy of pancreatic ductal adenocarcinoma, to MUC5AC mucin.

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

REVISTA / JOURNAL: - Mol Cancer. 2013 Nov 20;12(1):143.

●● Enlace al texto completo (gratuito o de pago) 1186/1476-4598-12-143

AUTORES / AUTHORS: - Gold DV; Newsome G; Liu D; Goldenberg DM

RESUMEN / SUMMARY: - BACKGROUND: PAM4, an antibody that has high specificity for pancreatic ductal adenocarcinoma (PDAC), compared to normal pancreas, benign lesions of the pancreas, and cancers originating from other tissues, is being investigated as a biomarker for early detection, as well as antibody-targeted imaging and therapy. Therefore, the identity of the antigen bound by this monoclonal antibody (MAb) can provide information leading to improved use of the antibody. Prior results suggested the antigen is a mucin-type glycoprotein rich in cysteine disulfide bridges that provide stable conformation for the PAM4-epitope. METHODS: Indirect and sandwich enzyme immunoassays (EIA) were performed to compare and contrast the reactivity of PAM4 with several anti-mucin antibodies having known reactivity to specific mucin species (e.g., MUC1, MUC4, MUC5AC, etc.). Studies designed to block reactivity of PAM4 with its specific antigen also were performed. RESULTS: We demonstrate that MAbs 2-11 M1 and 45 M1, each reactive with MUC5AC, are able to provide signal in a heterologous sandwich immunoassay where PAM4 is the capture antibody. Further, we identify MAbs 21 M1, 62 M1, and 463 M1, each reactive with MUC5AC, as inhibiting the reaction of PAM4 with its specific epitope. MAbs directed to MUC1, MUC3, MUC4, MUC16 and CEACAM6 are not reactive with PAM4-captured antigen, nor are they able to block the reaction of PAM4 with its antigen.

CONCLUSIONS: These data implicate MUC5AC as a specific mucin species to which PAM4 is reactive. Furthermore, this realization may allow for the improvement of the current PAM4 serum-based immunoassay for detection of early-stage PDAC by the application of anti-MUC5AC MAbs as probes in this sandwich EIA.

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[218]
TÍTULO / TITLE: - Electroacupuncture treatment for pancreatic cancer pain: A randomized controlled trial.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreatology. 2013 Nov-Dec;13(6):594-7. doi: 10.1016/j.pan.2013.10.007. Epub 2013 Oct 23.
●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.10.007
AUTORES / AUTHORS: - Chen H; Liu TY; Kuai L; Zhu J; Wu CJ; Liu LM
INSTITUCIÓN / INSTITUTION: - Department of Integrative Oncology, Fudan University Shanghai Cancer Center, Shanghai, China.
RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is often accompanied by severe abdominal or back pain. It's the first study to evaluate the analgesic effect of electroacupuncture on pancreatic cancer pain. A randomized controlled trial compared electroacupuncture with control acupuncture using the placebo needle. METHODS: Sixty patients with pancreatic cancer pain were randomly assigned to the electroacupuncture group (n = 30) and the placebo control group (n = 30). Patients were treated on Jiaji (Ex-B2) points T8-T12 bilaterally for 30 min once a day for 3 days. Pain intensity was assessed with numerical rated scales (NRS) before the treatment (Baseline), after 3 treatments, and 2 days follow-up. RESULTS: Baseline characteristics were similar in the two groups. After 3 treatment, pain intensity on NRS decreased compared with Baseline (-1.67, 95% confidence interval [CI] -1.46 to -1.87) in the electroacupuncture group; there was little change (-0.13, 95% CI 0.08 to -0.35) in control group; the difference between two groups was statistically significant (P < 0.001). Follow-up also found a significant reduction in pain intensity in the electroacupuncture group compared with the control group (P < 0.001). CONCLUSIONS: Electroacupuncture was an effective treatment for relieving pancreatic cancer pain.

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[219]
TÍTULO / TITLE: - Phase I/II clinical trial using HLA-A24-restricted peptide vaccine derived from KIF20A for patients with advanced pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Transl Med. 2013 Nov 16;11(1):291.
●● Enlace al texto completo (gratuito o de pago) 1186/1479-5876-11-291
AUTORES / AUTHORS: - Asahara S; Takeda K; Yamao K; Maguchi H; Yamaue H
RESUMEN / SUMMARY: - BACKGROUND: We previously developed an immunotherapy treatment utilizing a cancer vaccine reagent KIF20A-66 in order to treat pancreatic cancer. KIF20A-66 is HLA-A25-restricted epitope peptide derived from KIF20A, a member of kinesin super family protein 20A (KIF20A) that is significantly transactivated in pancreatic cancer. In this report, we further demonstrated non-randomized, open-label, single centered phase I/II clinical trial of immunotherapy using

the KIF20A-66 peptide for the patients with advanced pancreatic cancer. METHODS: Vaccination was performed to the patients with metastatic pancreatic cancer, in whom gemcitabine-based therapy had failed. In phase I study, KIF20A-66 peptide was subcutaneously injected weekly in a dose-escalation manner (doses of 1.0 and 3.0 mg/body, 6 patients/1 cohort). After safety was assessed, phase II study was conducted using 3.0 mg of KIF20A-66 peptide. RESULTS: KIF20A-66 peptide vaccination was well tolerated in the doses we examined and tumor responses after 1 month of the treatment were evaluated. Among 29 patients who completed one course of the treatment at least, stable disease (SD) was found in 21 cases, while progressive disease (PD) was found in 8 cases, indicating that the disease control rate was 72%. Objective tumor shrinkage was observed in 8 cases, including 1 case of complete response (CR). The median survival time (MST) and progression free survival time (PFS) were 142 days and 56 days, respectively. These results clearly demonstrate that overall survival of the patients was significantly prolonged, compared to the historical controls of 9 cases with unmatched HLA in the same hospital (MST: 83 days), as well as 81 cases in our and other hospitals (MST: 63 days). CONCLUSION: The patients vaccinated with KIF20A-66 peptide had better prognosis than the control group with best supportive care (BSC). Thus, we concluded that KIF20A-66 vaccination is significantly effective as an immunotherapy against advanced pancreatic cancer. KIF20A-66 peptide was well tolerable in the dose of either 1.0 mg or 3.0 mg/body, and effectively induced peptide-specific response of cytotoxic T lymphocyte (CTL). Further clinical study using this peptide is a promising approach for advanced pancreatic cancer to achieve high potential benefit for better prognosis.Clinical trial registration: UMIN-CTR, number UMIN000004919.

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[220]

TÍTULO / TITLE: - Clinical and Pathologic Features Influencing Survival in Patients Undergoing Pancreaticoduodenectomy for Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Nov 23.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2388-x

AUTORES / AUTHORS: - Weber CE; Bock EA; Hurtuk MG; Abood GJ; Pickleman J; Shoup M; Aranha GV

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Division of Surgical Oncology, Loyola University, Maywood, IL, USA.

RESUMEN / SUMMARY: - OBJECTIVE: The aim of the study was to determine the clinicopathological features that influence survival in patients with resected pancreatic ductal adenocarcinoma (PDA). METHODS: The study used a single institution retrospective review of patients undergoing pancreaticoduodenectomy (PD) for PDA from 1993 to 2010. RESULTS: Two hundred forty-six consecutive cases of resected PDA were identified: 128 males (52 %), median age 68 years. Median hospital length of stay was 8 days and 30-day mortality rate was 2.4 %. There were 101 (41.1 %) postoperative complications, 77 % of which were Dindo-Clavien Grade 3 or less. Overall survival was 85, 63, 25, and 15 % at 6 months, 1 year, 3 years, and 5 years, respectively, with a median survival of 17 months. Multivariate Cox proportional hazard modeling demonstrated lymph node ratio was negatively correlated with survival at all time points. Preoperative hypertension was a poor prognostic factor at 6 months, 3

years, and 5 years. The absence of postoperative complications was protective at 6 months whereas pancreatic leaks were associated with worse survival at 6 months. Abdominal pain on presentation, operative time, and estimated blood loss were also associated with decreased survival at various time points. CONCLUSION: The strongest prognostic variable for short- and long-term survival after PD for PDA is lymph node ratio. Short-term survival is influenced by the postoperative course.

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[221]

TÍTULO / TITLE: - Gemcitabine based neoadjuvant chemoradiotherapy therapy in patients with borderline resectable pancreatic cancer.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Sep-Oct;13(5):539-43. doi: 10.1016/j.pan.2013.07.064. Epub 2013 Jul 18.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.07.064

AUTORES / AUTHORS: - Cho IR; Chung MJ; Bang S; Park SW; Chung JB; Song SY; Seong J; Hwang HK; Kang CM; Lee WJ; Park JY

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology, Department of Internal Medicine and Yonsei Institute of Gastroenterology, Severance Hospital, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea.

RESUMEN / SUMMARY: - BACKGROUND: Surgical resection is the only curative treatment for pancreatic cancer, but surgical outcomes for borderline resectable pancreatic cancer (BRPC) are generally poor because of the complexity of the surgery and the advanced nature of the tumor. The aim of this study was to evaluate whether neoadjuvant concurrent chemoradiation therapy (CCRT) in BRPC patients could improve surgical outcome. METHODS: Baseline characteristics and treatment outcomes for patients who underwent surgery for BRPC with (CCRT (+) group) and without neoadjuvant treatment (CCRT (-) group) were retrospectively compared. Treatment outcomes measured included overall survival, recurrence-free survival, and perioperative complications. RESULTS: A total of 30 patients were included in the CCRT (+) group and 21 patients in the CCRT (-) group. Baseline characteristics were not different before CCRT, but pathological examination after resection revealed reduced tumor size and a lower neurovascular invasion rate in the CCRT (+) group. Overall median survival time was 45.0 months in the CCRT (+) group and 23.5 months in the CCRT (-) group ($p = 0.045$). The CCRT (+) group had a lower recurrence rate (50.0% vs. 81.0%; $p = 0.024$) and a longer median disease-free survival period (21.0 months vs. 10.6 months; $p = 0.004$) than the CCRT (-) group. Perioperative complication rates were not different between the two groups. CONCLUSIONS: Neoadjuvant chemoradiation therapy combined with surgical resection yielded better treatment outcomes in patients with BRPC compared with surgery alone. Further larger prospective clinical trials with well defined enrollment criteria and treatment plan are needed.

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[222]

TÍTULO / TITLE: - Elevated pre-operative neutrophil to lymphocyte ratio predicts disease free survival following pancreatic resection for periampullary carcinomas.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreatology. 2013 Sep-Oct;13(5):534-8. doi: 10.1016/j.pan.2013.07.283. Epub 2013 Jul 31.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.07.283

AUTORES / AUTHORS: - Hamed MO; Roberts KJ; Smith AM; Morris Stiff G
INSTITUCIÓN / INSTITUTION: - The Pancreatic Unit, St James's University Hospital, Beckett Street, Leeds LS9 7TF, UK.
RESUMEN / SUMMARY: - BACKGROUND: The pre-operative neutrophil-to-lymphocyte ratio (NLR), when >/=5 has been associated with reduced survival for patients with various gastrointestinal tract cancers, however, it's prognostic value in patients with periampullary tumour has not been reported to date. OBJECTIVES: To determine the prognostic value of pre-operative NLR in terms of survival and recurrence of resected periampullary carcinomas. METHODS: This was a retrospective cohort study of consecutive patients undergoing pancreatoduodenectomy (PD) for periampullary carcinoma (pancreatic, ampullary, cholangiocarcinoma) identified from a departmental database. The effect of NLR upon survival and recurrence was explored. RESULTS: Overall median survival amongst 228 patients was 24 months (inter-quartile range [IQR]: 12-43). The median survival for those whose NLR was <5 was not significantly greater than those patients whose NLR was >/=5 (24 months [IQR: 14-42] versus 13 months [IQR: 8-48], respectively; p = 0.234). However, for those that developed recurrence, survival was greater in those with an NLR <5 at (20 months [IQR: 12-27] versus 11 months [IQR: 7-22], respectively; p = 0.038). This effect was most marked in those patients with cholangiocarcinoma (p = 0.019) whilst a trend to worse survival was seen in those with pancreatic adenocarcinoma. No effect was seen in patients with ampullary carcinoma (p = 0.516). CONCLUSIONS: This study provides further evidence that pre-operative NLR offers important prognostic information regarding disease-free survival. This effect, however, is dependent upon the tumour type amongst patients undergoing PD.

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[223]
TÍTULO / TITLE: - Human equilibrative nucleoside transporter 1 (hENT1): Do we really have a new predictive biomarker of chemotherapy outcome in pancreatic cancer patients?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreatology. 2013 Nov-Dec;13(6):558-63. doi: 10.1016/j.pan.2013.09.005. Epub 2013 Oct 10.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.09.005

AUTORES / AUTHORS: - Mohelnikova-Duchonova B; Melichar B
INSTITUCIÓN / INSTITUTION: - Department of Oncology, Palacky University Medical School and Teaching Hospital, Olomouc, Czech Republic; Biomedical Centre, Faculty of Medicine in Plzen, Charles University in Prague, Plzen, Czech Republic. Electronic address: beatrice.mohelnikova@gmail.com.
RESUMEN / SUMMARY: - Although systemic chemotherapy significantly improves the overall survival of pancreatic cancer patients, the prognosis remains extremely poor. The development of a drug resistance, either de novo or induced resistance, significantly limits the effectiveness of chemotherapy. SLC29A1 gene encodes human equilibrative nucleoside transporter 1 (hENT1) protein that is mediating the transport of

nucleotides, both purines and pyrimidines, into the tumor cells. The aim of this mini-review is to summarize the current information concerning the prognostic and predictive role of SLC29A1 transporter (hENT1) expression in pancreatic cancer. Increased expression of SLC29A1 in vitro has been described as a potential critical factor determining the sensitivity of pancreatic cancer cells to gemcitabine and 5-fluorouracil, the principal cytotoxic agents used in the treatment of pancreatic cancer. The reports on the relationship between SLC29A1 expression and prognosis of patients with pancreatic cancer are currently rather conflicting. However, majority of studies on patients with resected pancreatic cancer have suggested that high SLC29A1expression may be predictive of improved survival in patients treated with gemcitabine. SLC29A1 has not been shown to represent a predictive biomarker for patients treated by 5-fluorouracil. In conclusion, potential prognostic and predictive role of SLC29A1 has been demonstrated for selected subset of patients.

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[224]

TÍTULO / TITLE: - Improvement of long-term outcomes in pancreatic cancer and its associated factors within the gemcitabine era: a collaborative retrospective multicenter clinical review of 1,082 patients.

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

REVISTA / JOURNAL: - BMC Gastroenterol. 2013 Aug 31;13:134. doi: 10.1186/1471-230X-13-134.

●● Enlace al texto completo (gratuito o de pago) 1186/1471-230X-13-134

AUTORES / AUTHORS: - Kuroda T; Kumagi T; Yokota T; Seike H; Nishiyama M; Imai Y; Inada N; Shibata N; Imamine S; Okada S; Koizumi M; Yamanishi H; Azemoto N; Miyaike J; Tanaka Y; Tatsukawa H; Utsunomiya H; Ohno Y; Miyake T; Hirooka M; Furukawa S; Abe M; Ikeda Y; Matsuura B; Hiasa Y; Onji M

RESUMEN / SUMMARY: - BACKGROUND: Although the outcomes of pancreatic cancer have been improved by gemcitabine, the changes in its characteristics and long-term outcomes within the gemcitabine era remain unclear. This study was conducted to identify clinical characteristics of pancreatic cancer patients within the gemcitabine era. METHODS: A retrospective chart review was performed at 10 centers for 1,248 consecutive patients who were ever considered to have a diagnosis of pancreatic cancer between 2001 and 2010. Data collected included demographics, diagnosis date, clinical stage, treatment, and outcome 1,082 patients met the inclusion criteria and were analyzed further. The chi-square test, Student's t-test, and Mann-Whitney U-test were used for statistical analysis. Outcomes were analyzed using the Kaplan-Meier method and Cox proportional hazards regression. Differences in survival analyses were determined using the log-rank test. RESULTS: The distribution of clinical stages was: I, 2.2% II, 3.4% III, 13% IVa, 27% and IVb, 55%. Chemotherapy alone was administered to 42% of patients and 17% underwent resection. The 1-, 3-, and 5-year survival rates were 39%, 13%, and 6.9%, respectively. The median survival time was 257 days, but differed considerably among treatments and clinical stages. Demographics, distribution of clinical stage, and cause of death did not differ between groups A (2001-2005, n=406) and B (2006-2010, n=676). However, group B included more patients who underwent chemotherapy (P<0.0001) and fewer treated with best supportive care (P=0.0004), mirroring improvements in this group's long-term outcomes (P=0.0063). Finally, factors associated with long-term outcomes derived

from multivariate analysis were clinical stage (P<0.0001), location of the tumor (P=0.0294) and treatments (surgery, chemotherapy) (<0.0001). CONCLUSIONS: Long-term outcomes in pancreatic cancer has improved even within the gemcitabine era, suggesting the importance of offering chemotherapy to patients previously only considered for best supportive care. Most patients are still diagnosed at an advanced stage, making clinical strategy development for diagnosing pancreatic cancer at earlier stages essential.

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[225]

TÍTULO / TITLE: - Treatment Sequencing for Resectable Pancreatic Cancer: Influence of Early Metastases and Surgical Complications on Multimodality Therapy Completion and Survival.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Nov 16.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2412-1

AUTORES / AUTHORS: - Tzeng CW; Cao HS; Lee JE; Pisters PW; Varadhachary GR; Wolff RA; Abbruzzese JL; Crane CH; Evans DB; Wang H; Abbott DE; Vauthey JN; Aloia TA; Fleming JB; Katz MH

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Kentucky, Lexington, KY, USA.

RESUMEN / SUMMARY: - Barriers to multimodality therapy (MMT) completion among patients with resectable pancreatic adenocarcinoma include early cancer progression and postoperative major complications (PMC). We sought to evaluate the influence of these factors on MMT completion rates of patients treated with neoadjuvant therapy (NT) and surgery-first (SF) approaches. We evaluated all operable patients treated for clinically resectable pancreatic head adenocarcinoma at our institution from 2002 to 2007. Rates of MMT completion, 90-day PMC, and overall survival (OS) were evaluated. Ninety-five of 115 (83 %) NT and 29/50 (58 %) SF patients completed MMT. Patients who completed MMT lived longer than those who did not (36 vs. 11 months, p < 0.001). The most common reason that NT (11 %) and SF (26 %) patients failed to complete MMT was early disease progression. The rates of PMC among NT and SF patients were similar. Among SF patients, 69 % with no PMC completed MMT versus 29 % after PMC (p = 0.040). PMC were associated with decreased OS in SF patients but not in NT patients. The impact of early cancer progression and PMC upon completion of MMT is reduced by delivery of nonoperative therapies prior to pancreaticoduodenectomy. NT sequencing is a practical treatment strategy, particularly for patients at high biological or perioperative risk.

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[226]

TÍTULO / TITLE: - Overexpressing TNF-Alpha in Pancreatic Ductal Adenocarcinoma Cells and Fibroblasts Modifies Cell Survival and Reduces Fatty Acid Synthesis via Downregulation of Sterol Regulatory Element Binding Protein-1 and Activation of Acetyl CoA Carboxylase.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Oct 4.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2370-7

AUTORES / AUTHORS: - Al-Zoubi M; Chipitsyna G; Saxena S; Sarosiek K; Gandhi A; Kang CY; Relles D; Andrelsendecki J; Hyslop T; Yeo CJ; Arafat HA

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The Jefferson Pancreatic, Biliary and Related Cancer Center, Thomas Jefferson University, 1015 Walnut Street, Suite 618 Curtis, Philadelphia, PA, 19107, USA.

RESUMEN / SUMMARY: - The effect of tumor necrosis factor-alpha (TNF-alpha) gene delivery has been suggested as a potentially useful therapeutic approach to improve the chemotherapeutic treatment of patients with pancreatic ductal adenocarcinoma (PDA), but the exact mechanism of its action is not clearly understood. In this study, we analyzed the expression profile of TNF-alpha in PDA tissue and explored its potential role in fatty acid synthase (FAS) regulation in PDA cells and in fibroblasts. Quantitative real-time polymerase chain reaction was used to examine the expression of TNF-alpha in PDA, matching adjacent tissues, and benign lesions. Logistic regression models with robust variance were used to analyze the gene expression levels, and Kaplan-Meier survival curves were generated. In vitro, we overexpressed the TNF-alpha gene in PDA cells and fibroblasts and analyzed its effect on cell survival, migration, and on members of the FAS signaling pathway. We also evaluated TNF-alpha effects on a panel of inflammation-, angiogenesis-, and metastasis-related markers. In the tumor tissue of PDA patients, compared with their matched adjacent tissue, expression levels of TNF-alpha were not statistically different and did not correlate with survival or any other examined clinicopathological features. Overexpression of TNF-alpha significantly ($p < 0.05$) reduced PDA and fibroblast cell migration. In PDA cells that highly overexpress TNF-alpha, this was associated with a significant reduction of FAS mRNA and protein expression levels and significant ($p < 0.05$) reduction of SREBP-1 and ACC mRNA. Reduction of FAS by TNF-alpha was inhibited when either SREBP-1 or ACC was knocked down by siRNA. PDA cells and fibroblasts that overexpress TNF-alpha displayed differential regulation of several inflammation-related markers and reduced levels of metastasis-related genes. Our data demonstrate a previously unknown multi-targeted involvement of TNF-alpha in PDA lipogenesis and inflammation and metastasis and suggest that intratumoral introduction of TNF-alpha may have the potential as a novel therapeutic approach in human PDA.

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[227]

TÍTULO / TITLE: - Comprehensive analysis of the percentage of surface receptors and cytotoxic granules positive natural killer cells in patients with pancreatic cancer, gastric cancer, and colorectal cancer.

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

REVISTA / JOURNAL: - J Transl Med. 2013 Oct 20;11(1):262.

●● Enlace al texto completo (gratuito o de pago) 1186/1479-5876-11-262

AUTORES / AUTHORS: - Peng YP; Zhu Y; Zhang JJ; Xu ZK; Qian ZY; Dai CC; Jiang KR; Wu JL; Gao WT; Li Q; Du Q; Miao Y

RESUMEN / SUMMARY: - BACKGROUND: Digestive malignancies, especially pancreatic cancer (PC), gastric cancer (GC), and colorectal cancer (CRC), still occur at persistently high rates, and disease progression in these cancers has been associated with tumor immunosurveillance escape. Natural killer (NK) cell dysfunction may be responsible for this phenomenon, however, the exact relationship between tumor immunosurveillance escape in digestive malignancies and NK cell dysfunction remains

unclear. METHODS: Percentage of the surface receptors NKG2A, KIR3DL1, NKG2D, NKp30, NKp44, NKp46, and DNAM-1, as well as the cytotoxic granules perforin and granzyme B positive NK cells were determined in patients with pancreatic cancer (n = 31), gastric cancer (n = 31), and CRC (n = 32) prior to surgery and healthy controls (n = 31) by multicolor flow cytometry. Independent t-tests or Mann-Whitney U-tests were used to compare the differences between the patient and healthy control groups, as well as the differences between patients with different pathologic features of cancer. RESULTS: Percentage of NKG2D, NKp30, NKp46, and perforin positive NK cells was significantly down-regulated in patients with PC compared to healthy controls, as well as GC and CRC; reduced levels of these molecules was associated with indicators of disease progression in each malignancy (such as histological grade, depth of invasion, lymph node metastasis). On the contrary, percentage of KIR3DL1 positive NK cells was significantly increased in patients with PC, as well as GC and CRC, but was not associated with any indicators of disease progression. CONCLUSIONS: Altered percentage of surface receptors and cytotoxic granules positive NK cells may play a vital role in tumor immunosurveillance escape by inducing NK cell dysfunction in patients with PC, GC, and CRC.

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[228]

TÍTULO / TITLE: - Synergistic Activities of MET/RON Inhibitor BMS-777607 and mTOR inhibitor AZD8055 to Polyploid Cells Derived from Pancreatic Cancer and Cancer Stem Cells.

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

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Nov 14.

●● Enlace al texto completo (gratuito o de pago) 1158/1535-7163.MCT-13-0242

AUTORES / AUTHORS: - Zeng JY; Sharma S; Zhou YQ; Yao HP; Hu X; Zhang R; Wang MH

INSTITUCIÓN / INSTITUTION: - 1Biomedical/Pharmaceutical Sciences, Texas Tech University Health Sciences Center.

RESUMEN / SUMMARY: - Tyrosine kinase inhibitor BMS-777067 is an inhibitor of RON/MET receptor tyrosine kinases currently under clinical trials. Here, we report the synergistic activity of BMS-777607 in combination with mTOR inhibitor AZD8055 in killing chemoresistant pancreatic cancer and cancer stem cells. Treatment of pancreatic cancer L3.6pl cells with BMS-777607 alone inhibited clonogenic growth and moderately induced apoptotic death. However, BMS-777607 caused extensive polyploidy in L3.6pl cells through inhibition of aurora kinase B activity, independent of RON expression. In contrast, L3.6pl-derived cancer stem cells were highly resistant to BMS-777607-induced growth inhibition and apoptosis. The effect of BMS-777607 on induction of cancer stem cell polyploidy also was weak. BMS-777607-induced polyploidy features a predominant cell population with 8N chromosome content in both L3.6pl and cancer stem cells. These cells also showed decreased sensitivity towards chemotherapeutics by increased survival of IC50 values in response to doxorubicin, cisplatin, methotrexate, 5-fluorouracial, and gemcitabine. Among a panel of chemical inhibitors that target different signaling proteins, we found that BMS-777607 in combination with mTOR inhibitor AZD8055 exerted synergistic effects on L3.6pl and cancer stem cells. More than 70% of L3.6pl and cancer stem cells lost their viability

when both inhibitors were used. Specifically, BMS-777607 in combination with inhibition of mTORC2 but not mTORC1 was responsible for the observed synergism. Our findings demonstrate that BMS-777607 at therapeutic doses exerts inhibitory activities on pancreatic cancer cells but also induces polyploidy insensitive to chemotherapeutics. Combination of BMS-777607 with AZD8055 achieves the maximal cytotoxic effect on pancreatic cancer and cancer stem cells.

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[229]

TÍTULO / TITLE: - Chemoradiation for resected pancreatic adenocarcinoma with or without intraoperative radiation therapy boost: Long-term outcomes.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Nov-Dec;13(6):576-82. doi: 10.1016/j.pan.2013.09.002. Epub 2013 Sep 30.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.09.002

AUTORES / AUTHORS: - Calvo FA; Sole CV; Atahualpa F; Lozano MA; Gomez-Espi M; Calin A; Garcia-Alfonso P; Gonzalez-Bayon L; Herranz R; Garcia-Sabrido JL

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Hospital General Universitario Gregorio Maranon, Madrid, España; School of Medicine, Complutense University, Madrid, España.

RESUMEN / SUMMARY: - BACKGROUND/OBJECTIVES: To analyze prognostic factors associated with long-term outcomes in patients with pancreatic cancer treated with chemoradiation therapy (CRT) and surgery with or without intraoperative electron beam radiotherapy (IOERT). PATIENTS AND METHODS: From January 1995 to December 2012, 60 patients with adenocarcinoma of the pancreas and locoregional disease (clinical stage IB [n = 13; 22%], IIA [n = 16; 27%], IIB [n = 22; 36%], IIIC [n = 9; 15%]) were treated with CRT (45-50.4 Gy before surgery [n = 19; 32%] and after surgery [n = 41; 68%]) and curative resection (R0 [n = 34; 57%], R1 [n = 26, 43%]). Twenty-nine patients (48%) also received a pre-anastomosis IOERT boost (applicator diameter size, 7-10 cm; dose, 10-15 Gy; beam energy, 9-18 MeV). RESULTS: With a median follow-up of 15.9 months (range, 1-182), 5-year overall survival (OS), disease-free survival (DFS), and locoregional control were 20%, 13%, and 58%, respectively. Univariate analyses showed that R1 margin resection status (HR, 3.17; p = 0.04), not receiving IOERT (HR, 7.33; p = 0.01), and postoperative CRT (HR, 5.12; p = 0.04) were associated with a higher risk of locoregional recurrence. In the multivariate analysis, only margin resection status (HR, 3.0; p = 0.05) and not receiving IOERT (HR, 6.75; p = 0.01) retained significance with regard to locoregional recurrence. Postoperative mortality and perioperative complications were 3% (n = 2) and 43% (n = 26). CONCLUSIONS: Although local control is good in the radiation-boosted area, OS remains modest owing to high risk of distant metastases. Intensified locoregional treatment needs to be tested in the context of more efficient systemic therapy.

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[230]

TÍTULO / TITLE: - Change of fucosylated IgG Fc-glycoforms in pancreatitis and pancreatic adenocarcinoma: a promising disease-classification model.

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

REVISTA / JOURNAL: - Anal Bioanal Chem. 2013 Nov 5.

●● Enlace al texto completo (gratuito o de pago) 1007/s00216-013-7439-3

AUTORES / AUTHORS: - Chen G; Li H; Qiu L; Qin X; Liu H; Li Z

INSTITUCIÓN / INSTITUTION: - Department of Biophysics and Structural Biology, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences and Peking Union Medical College, 5 Dongdan San Tiao, Beijing, 100005, China.

RESUMEN / SUMMARY: - The fixed constant (Fc) region of IgG is subject to changes in glycosylation state in response to diseases. On the basis of sera from 75 healthy controls, 75 pancreatitis (PT) patients, and 75 pancreatic adenocarcinoma (PAC) patients, we analyzed six fucosylated glycoforms of IgG2 (G0F, G1F, G2F, G0FN, G1FN, and G2FN), by matrix-assisted laser desorption/ionization-Fourier-transform ion cyclotron resonance mass spectrometry (MALDI-FTICR MS), to evaluate their use as biomarkers for pancreatic diseases. Compared with healthy controls, significant increases in agalactosylated glycoforms and decreases in galactosylated glycoforms were observed for PT and PAC patients. Logistic regression analysis suggested that truncation of the sugar chain was prone to occur in PT and, especially, PAC patients. After participants were stratified by sex and age, receiver operating characteristic curve analysis revealed good overall sensitivity and specificity for discrimination of PAC and PT patients from healthy controls. A combination of G0F and galactosylation also had acceptable power for differentiating PAC patients from PT patients.

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[231]

TÍTULO / TITLE: - Radiolabelled somatostatin analogue treatment in gastroenteropancreatic neuroendocrine tumours: factors associated with response and suggestions for therapeutic sequence: response to comments by Ezziddin et al.

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

REVISTA / JOURNAL: - Eur J Nucl Med Mol Imaging. 2014 Jan;41(1):176-7. doi: 10.1007/s00259-013-2603-8.

●● Enlace al texto completo (gratuito o de pago) 1007/s00259-013-2603-8

AUTORES / AUTHORS: - Campana D; Delle Fave G; Falconi M; Tommassetti P

INSTITUCIÓN / INSTITUTION: - Department of Medical and Surgical Sciences, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy, davide.campana@unibo.it.

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[232]

TÍTULO / TITLE: - Comment on Campana et al.: Radiolabelled somatostatin analogue treatment in gastroenteropancreatic neuroendocrine tumours: factors associated with response and suggestions for therapeutic sequence.

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

REVISTA / JOURNAL: - Eur J Nucl Med Mol Imaging. 2014 Jan;41(1):174-5. doi: 10.1007/s00259-013-2599-0. Epub 2013 Nov 6.

●● Enlace al texto completo (gratuito o de pago) 1007/s00259-013-2599-0

AUTORES / AUTHORS: - Ezziddin S; Sabet A; Yong-Hing CJ; Biersack HJ

INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, University Hospital Bonn, Sigmund-Freud-Str. 25, 53105, Bonn, Germany, samer.ezziddin@ukb.uni-bonn.de.

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[233]

TÍTULO / TITLE: - Loss of HAI-1 participates in metastatic spreading of human pancreatic cancer cells in a mouse orthotopic transplantation model.

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

REVISTA / JOURNAL: - Cancer Sci. 2013 Oct 22. doi: 10.1111/cas.12306.

●● Enlace al texto completo (gratuito o de pago) 1111/cas.12306

AUTORES / AUTHORS: - Ye J; Kawaguchi M; Haruyama Y; Kanemaru A; Fukushima T; Yamamoto K; Lin CY; Kataoka H

INSTITUCIÓN / INSTITUTION: - Section of Oncopathology and Regenerative Biology, Department of Pathology, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan; Clinical Research Center, The 2nd Affiliated Hospital School of Medicine, Zhejiang University, Hangzhou, P. R. China.

RESUMEN / SUMMARY: - Hepatocyte growth factor activator inhibitor type 1 (HAI-1) is a membrane-bound serine protease inhibitor that is expressed on the surface of epithelial and carcinoma cells. On the cell surface, HAI-1 regulates membrane-anchored serine proteases with matriptase being the most critical target. Matriptase is involved in pericellular processing of biologically active molecules, including protease-activated receptor-2 (PAR-2). Previously we reported that S2-CP8 cells, a metastatic variant of the SUIT-2 human pancreatic adenocarcinoma cell line, showed markedly decreased HAI-1 expression. To assess the significance of HAI-1 loss in invasion and spontaneous metastasis of S2-CP8 cells, we established stable S2-CP8 sublines that expressed HAI-1 under the control of a tetracycline-regulated promoter. In vitro migration and Matrigel invasion assays revealed inhibitory effects of HAI-1 on S2-CP8 cell migration and invasion. Matriptase activity was suppressed by the expression of HAI-1. As the enhanced invasiveness in the absence of HAI-1was alleviated by knockdown of matriptase by 81% and of PAR-2 completely and PAR-2 antagonist also suppressed the invasion, matriptase-mediated PAR-2 activation is involved in HAI-1 loss-induced invasion of S2-CP8 cells. We then analyzed the effect of HAI-1 expression on metastasis of S2-CP8 cells in vivo using a nude mouse orthotopic xenograft model. Although about 50% of control mice developed distant metastasis, mice treated with doxycycline to induce HAI-1 expression did not develop metastasis. These data indicate that HAI-1 loss contributes to invasion and dissemination of a highly metastatic subline of SUIT-2, suggesting crucial roles for the balance of pericellular serine proteases/inhibitors in pancreatic cancer progression. This article is protected by copyright. All rights reserved.

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[234]

TÍTULO / TITLE: - The status of HBV infection influences metastatic pattern and survival in Chinese patients with pancreatic cancer.

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

REVISTA / JOURNAL: - J Transl Med. 2013 Oct 8;11(1):249. doi: 10.1186/1479-5876-11-249.

●● Enlace al texto completo (gratuito o de pago) 1186/1479-5876-11-249

AUTORES / AUTHORS: - Wei XL; Qiu MZ; Chen WW; Jin Y; Ren C; Wang F; Luo HY; Wang ZQ; Zhang DS; Wang FH; Li YH; Xu RH

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Oncology in South China, Department of Medical Oncology, Collaborative Innovation Center of Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou 510060, China. xurh@sysucc.org.cn.

RESUMEN / SUMMARY: - BACKGROUND: It has been proved that hepatitis B virus (HBV) infection alters the metastatic pattern and affects survival in colorectal cancer (CRC) and hepatocellular carcinoma (HCC), while the influence of HBV infection on metastatic pattern and survival in patients with pancreatic cancer (PC) has not been investigated yet. METHODS: We conducted an investigation to evaluate the impact of HBV infection on metastatic pattern and overall survival in PC. We collected the data of 460 PC patients treated in our hospital from 1999 to 2010. Serum HBV markers were tested with enzyme-linked immunosorbent assay. The impact of HBV infection on metastatic pattern and overall survival was analyzed. RESULTS: We found that the incidence of synchronous liver metastasis was significantly higher in patients with HBsAg positive than those with HBsAg negative (46.0% vs 32.0%, P < 0.05), and higher in chronic HBV infection (CHB) group than both non HBV infection and resolved HBV infection group (61.1% vs 33.9%, P < 0.05, and 61.1% vs 28.7%, P < 0.05, respectively). What's more, Kaplan-Meier analysis showed that CHB, resolved HBV infection and non HBV infection group had significant longer overall survival (OS) compared with inactive HBsAg carriers (IC) group (P=0.037, P=0.009, and P=0.019 respectively). But, in the multivariate analysis, only the CHB and non HBV infection group had significant better overall survival compared with IC group (P=0.010 and P=0.018 respectively). CONCLUSIONS: Our study found that HBV infection increased synchronous liver metastasis rate, and HBV infection status was an independent prognostic factor in PC patients.

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[235]

TÍTULO / TITLE: - Chemoprevention gene therapy (CGT) of pancreatic cancer using perillyl alcohol and a novel chimeric serotype Cancer Terminator Virus.

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

REVISTA / JOURNAL: - Curr Mol Med. 2013 Nov 17.

AUTORES / AUTHORS: - Sarkar S; Azab B; Quinn BA; Shen X; Dent P; Klibanov AL; Emdad L; Das SK; Sarkar D; Fisher PB

INSTITUCIÓN / INSTITUTION: - Department of Human and Molecular Genetics, Virginia Commonwealth University, School of Medicine, P.O. Box 980678, Richmond, VA 23298-067, USA. pbfisher@vcu.edu.

RESUMEN / SUMMARY: - Conditionally replication competent adenoviruses (Ads) that selectively replicate in cancer cells and simultaneously express a therapeutic cytokine, such as melanoma differentiation associated gene-7/Interleukin-24 (mda-7/IL-24), a Cancer Terminator Virus (CTV-M7), hold potential for treating human cancers. To enhance the efficacy of the CTV-M7, we generated a chimeric Ad.5 and Ad.3 modified fiber bipartite CTV (Ad.5/3-CTV-M7) that can infect tumor cells in a Coxsackie Adenovirus receptor (CAR) independent manner, while retaining high infectivity in cancer cells containing high CAR. Although mda-7/IL-24 displays broad-spectrum anticancer properties, pancreatic ductal adenocarcinoma (PDAC) cells display an intrinsic resistance to mda-7/IL-24-mediated killing due to an mda-7/IL-24 mRNA translational block. However, using a chemoprevention gene therapy (CGT) approach

with perillyl alcohol (POH) and a replication incompetent Ad to deliver mda-7/IL-24 (Ad.mda-7) there is enhanced conversion of mda-7/IL-24 mRNA into protein resulting in pancreatic cancer cell death in vitro and in vivo in nude mice containing human PDAC xenografts. This combination synergistically induces mda-7/IL-24-mediated cancer-specific apoptosis by inhibiting anti-apoptotic Bcl-xL and Bcl-2 protein expression and inducing an endoplasmic reticulum (ER) stress response through induction of BiP/GRP-78, which is most evident in chimeric-modified non-replicating Ad.5/3-mda-7- and CTV-M7-infected PDAC cells. Moreover, Ad.5/3-CTV-M7 in combination with POH sensitizes therapy-resistant MIA PaCa-2 cell lines over-expressing either Bcl-2 or Bcl-xL to mda-7/IL-24-mediated apoptosis. Ad.5/3-CTV-M7 plus POH also exerts a significant antitumor 'bystander' effect in vivo suppressing both primary and distant site tumor growth, confirming therapeutic utility of Ad.5/3-CTV-M7 plus POH in PDAC treatment, where all other current treatment strategies in clinical settings show minimal efficacy.

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[236]

TÍTULO / TITLE: - Surface plasmon resonance-induced photoactivation of gold nanoparticles as mitochondria-targeted therapeutic agents for pancreatic cancer.

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

REVISTA / JOURNAL: - Expert Opin Ther Targets. 2013 Dec;17(12):1383-93. doi: 10.1517/14728222.2013.855200. Epub 2013 Nov 5.

●● Enlace al texto completo (gratuito o de pago) 1517/14728222.2013.855200

AUTORES / AUTHORS: - Mocan L; Ilie I; Tabaran FA; Dana B; Zaharie F; Zdrehus C; Puia C; Mocan T; Muntean V; Teodora P; Ofelia M; Marcel T; Iancu C

INSTITUCIÓN / INSTITUTION: - "Iuliu Hatieganu" University of Medicine and Pharmacy, Regional Institute of Gastroenterology and Hepatology, Department of Nanomedicine , Croitorilor Street, Cluj-Napoca , Romania , +40264-439696 ; +40264-439696 ; cornel.iancu@umfcluj.ro.

RESUMEN / SUMMARY: - Background: Noble metal nanoparticles such as gold nanoparticles can strongly absorb light in the visible region by inducing coherent collective oscillation of conduction band electrons in strong resonance with visible frequencies of light. This phenomenon is frequently termed as surface plasmon resonance (SPR). Objectives: The main objective was to study the effects of laser photoactivated gold nanoparticles (by means of SPR) on human pancreatic cancer cells. Results: Gold nanoparticles obtained using standard wet chemical methods (with sodium borohydride as a reducing agent) underwent photoexcitation using 2w 808 nm laser and further administered to 1.4E7 pancreatic cancer cell lines. Flow cytometry, transmission electron microscopy, phase contrast microscopy, quantitative proteomics and confocal microscopy combined with immunochemical staining were used to examine the interaction between photo excited gold nanoparticles and pancreatic cancer cells. Conclusion: The study shows that phonon-phonon interactions following laser photoexcitation of gold nanoparticles exhibit increased intracellular uptake, as well as mitochondrial swelling, closely followed by mitochondrial inner membrane permeabilization and depolarization. This unique data may represent a major step in mitochondria-targeted anticancer therapies using laser-activated gold nanoparticles.

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[237]
TÍTULO / TITLE: - Combined heterotopic liver-pancreas transplantation as a curative treatment for liver cirrhosis and diabetes mellitus in cystic fibrosis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pediatr Transplant. 2013 Oct 18. doi: 10.1111/petr.12157.
●● Enlace al texto completo (gratuito o de pago) 1111/petr.12157
AUTORES / AUTHORS: - Henn C; Kapellen T; Prenzel F; Siekmeyer M; Hau HM; Kiess W; Bartels M
INSTITUCIÓN / INSTITUTION: - Department of Women and Child Health, Hospital for Children and Adolescents, University Hospital Leipzig, Leipzig, Germany.
RESUMEN / SUMMARY: - Cystic fibrosis (CF) is an inherited disease with a defect in epithelial chloride transport that results in a multisystem disease. Although pulmonary disease remains the primary cause of morbidity and mortality, focal biliary cirrhosis and portal hypertension may develop in up to 8% of these patients. Liver transplantation (TX) is an accepted therapy and shows good results. We report on a patient with cystic fibrosis homozygous for the most common CFTR mutation delta F 508 who received a combined heterotopic liver and pancreas transplantation at the age of 18 yr. He suffered from CFRD, which untypically required high doses of insulin. In addition, the patient had pulmonary complications, was chronically colonized with multiresistant Pseudomonas aeruginosa (MBL) and had an allergic bronchopulmonary aspergillosis (ABPA). The patient remained in stable health for 54 months post-TX and was able to live a nearly normal life. With a follow-up of five yr, the function of the liver and pancreas allografts was excellent. However, and sadly, his pulmonary function continued to deteriorate from progression of his CF, and he died of respiratory failure due to a severe pneumonia and septicemia at the age of 23 yr and five months.

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[238]
TÍTULO / TITLE: - Is the detection of circulating tumor cells in locally advanced pancreatic cancer a useful prognostic marker?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Expert Rev Mol Diagn. 2013 Nov;13(8):793-6. doi: 10.1586/14737159.2013.845091. Epub 2013 Oct 16.
●● Enlace al texto completo (gratuito o de pago) 1586/14737159.2013.845091
AUTORES / AUTHORS: - Gall TM; Frampton AE; Krell J; Jacob J; Stebbing J; Jiao LR
INSTITUCIÓN / INSTITUTION: - Deptartment of Surgery & Cancer, HPB Surgical Unit, Imperial College, Hammersmith Hospital campus, Du Cane Road, London, W12 0HS, UK.
RESUMEN / SUMMARY: - Evaluation of: Bidard FC, Huguet F, Louvet C et al. Circulating tumor cells in locally advanced pancreatic adenocarcinoma: the ancillary CirCe 07 study to the LAP 07 trial. Ann. Oncol. 24(8), 2057-2061 (2013). Circulating tumor cells (CTCs) may be shed from the primary tumor and lead to metastatic disease. This evaluated article reports on CTCs in locally advanced pancreatic cancer (LAPC). By assessing CTCs from peripheral blood prior to any treatment and after 2 months of chemotherapy, 11% of patients had detectable CTCs. These patients had a poorer overall survival. With such low numbers of CTCs detected in LAPC patients, it is unclear whether CTCs can actually contribute toward tumor invasiveness and spread in such an aggressive cancer. Although this is a well-designed study, the small number of

patients with detectable CTCs means that the statistical power is not great enough to make firm conclusions. Therefore, this expensive assay needs further investigation before being used a prognostic marker in patients with LAPC.

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[239]

TÍTULO / TITLE: - Genetic and molecular alterations in pancreatic cancer: Implications for personalized medicine.

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

REVISTA / JOURNAL: - Med Sci Monit. 2013 Oct 31;19:916-26. doi: 10.12659/MSM.889636.

●● Enlace al texto completo (gratuito o de pago) 12659/MSM.889636

AUTORES / AUTHORS: - Fang Y; Yao Q; Chen Z; Xiang J; William FE; Gibbs RA; Chen C

INSTITUCIÓN / INSTITUTION: - Molecular Surgeon Research Center, Division of Surgical Research, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX, U.S.A. and Department of General Surgery, Huashan Hospital, Fudan University, Shanghai, P.R. China.

RESUMEN / SUMMARY: - Recent advances in human genomics and biotechnologies have profound impacts on medical research and clinical practice. Individual genomic information, including DNA sequences and gene expression profiles, can be used for prediction, prevention, diagnosis, and treatment for many complex diseases. Personalized medicine attempts to tailor medical care to individual patients by incorporating their genomic information. In a case of pancreatic cancer, the fourth leading cause of cancer death in the United States, alteration in many genes as well as molecular profiles in blood, pancreas tissue, and pancreas juice has recently been discovered to be closely associated with tumorigenesis or prognosis of the cancer. This review aims to summarize recent advances of important genes, proteins, and microRNAs that play a critical role in the pathogenesis of pancreatic cancer, and to provide implications for personalized medicine in pancreatic cancer.

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[240]

TÍTULO / TITLE: - Impact of endoscopic ultrasound-guided fine-needle aspiration on incidental pancreatic cysts. A prospective study.

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

REVISTA / JOURNAL: - Scand J Gastroenterol. 2013 Nov 5.

●● Enlace al texto completo (gratuito o de pago) 3109/00365521.2013.854830

AUTORES / AUTHORS: - Ardengh JC; Lopes CV; de Lima-Filho ER; Kemp R; Santos JS

INSTITUCIÓN / INSTITUTION: - Division of Surgery and Anatomy, Ribeirao Preto Medical School - University of Sao Paulo , Sao Paulo , Brazil.

RESUMEN / SUMMARY: - Abstract Objective. Widespread use of imaging procedures has promoted a higher identification of incidental pancreatic cysts (IPCs). However, little is known as to whether endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) could change the management strategy of patients having IPCs. This study has aimed to evaluate the management impact of EUS-FNA on IPCs. Material and methods. Patients with pancreatic cysts (PCs) who were referred to EUS-FNA were

recruited prospectively. The referring physicians were questioned about the management strategy for these patients before and after EUS-FNA. The impact of EUS-FNA on management was then evaluated. Results. A total of 302 PC patients were recruited. Of these, 159 (52.6%) patients had asymptomatic IPCs. The average size was 2.3 cm (range: 0.2-7.1 cm), and 110 patients having smaller than 3 cm sized cysts. Lesions were located in the pancreatic head in 96 (61%) cases, and most patients (94%) had only a single cyst. The final diagnoses, obtained by EUS-FNA (91) and surgery (68), were 93 (58%) benign lesions, 36 (23%) cysts with malignant potential, 14 (9%) noninvasive malignancies, 10 (6%) malignant precursor lesions (PanIN), and 6 (4%) invasive malignancies. Management strategy changed significantly after EUS-FNA in 114 (71.7%) patients: 43% of the cases were referred to surgery, 44% of the patients were discharged from surveillance, and 13% of the cases were given further periodical imaging tests. Conclusion. EUS-FNA has a management impact in almost 72% of IPCs, with a major influence on the management strategy, either discharge rather than surgical resection or surgery rather than additional follow up.

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[241]

TÍTULO / TITLE: - Redirecting Apoptosis to Aponecrosis Induces Selective Cytotoxicity to Pancreatic Cancer Cells through Increased ROS, Decline in ATP Levels, and VDAC.

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

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Nov 19.

●● Enlace al texto completo (gratuito o de pago) 1158/1535-7163.MCT-13-0234

AUTORES / AUTHORS: - Dinnen RD; Mao Y; Qiu W; Cassai N; Slavkovich VN; Nichols G; Su GH; Brandt-Rauf P; Fine RL

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: 1Experimental Therapeutics Program, Division of Medical Oncology, The Pancreas Center at Columbia; 2Department Pathology and Otolaryngology, Herbert Irving Cancer Center, Columbia University, College of Physicians and Surgeons; 3Department of Pathology and Laboratory Medicine, Harbor VA Medical Center, SUNY Downstate Medical Center, Brooklyn, New York; 4Department Environmental Health Science, Columbia University, New York; and 5University of Illinois School of Public Health, University of Illinois, Chicago, Illinois.

RESUMEN / SUMMARY: - Pancreatic cancer cell lines with mutated ras underwent an alternative form of cell death (aponecrosis) when treated concomitantly with clinically achievable concentrations of arsenic trioxide, ascorbic acid, and disulfiram (Antabuse; AAA). AAA's major effects are mediated through generation of intracellular reactive oxygen species (ROS) and more than 50% decline in intracellular ATP. N-acetyl cysteine and a superoxide dismutase mimetic prevented aponecrosis and restored intracellular ATP levels. DIDS (4,4'-diisothiocyanatostilbene-2, 2' disulfonic acid), the pan- Voltage-Dependent Anion Channel (VDAC), -1, 2, 3 inhibitor and short hairpin RNA (shRNA) to VDAC-1 blocked cell death and ROS accumulation. In vivo exposure of AAA led to a 62% reduction in mean tumor size and eliminated tumors in 30% of nude mice with PANC-1 xenografts. We concluded that early caspase-independent apoptosis was shifted to VDAC-mediated "targeted" aponecrosis by the addition of disulfiram to arsenic trioxide and ascorbic acid. Conceptually, this work represents a

paradigm shift where switching from apoptosis to aponecrosis death pathways, also known as targeted aponecrosis, could be utilized to selectively kill pancreatic cancer cells resistant to apoptosis. Mol Cancer Ther; 12(12); 1-12. ©2013 AACR.

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[242]

TÍTULO / TITLE: - Treatment of pancreatic cancer: A narrative review of cost-effectiveness studies.

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

REVISTA / JOURNAL: - Best Pract Res Clin Gastroenterol. 2013 Dec;27(6):881-92. doi: 10.1016/j.bpg.2013.09.006. Epub 2013 Oct 1.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bpg.2013.09.006

AUTORES / AUTHORS: - Bardou M; Le Ray I

INSTITUCIÓN / INSTITUTION: - Centre d'Investigations Cliniques plurithematique 803, INSERM CIC-P 803, CHU Dijon, Dijon Cedex, France; Centre de Recherche Lipides, Nutrition Cancer U866, INSERM - Institut National de la Sante et de la Recherche Medicale, Dijon Cedex, France; Universite de Bourgogne, Dijon Cedex, France. Electronic address: Marc.bardou@u-bourgogne.fr.

RESUMEN / SUMMARY: - Cancer of the pancreas is the second most frequent digestive cancer in the US, accounting for about 44,000 new cases per year. In Europe, it is the sixth most frequent cancer, accounting for 2.8% of cancers in men and 3.2% in women. With a five-year survival of less than 10%, it is the fifth leading cause of cancer-related death. The majority of cases are diagnosed above the age of 65 and in about 60% of cases at an advanced stage, explaining that little improvement has been observed in survival over the past 30 years. Radical surgery offers the only curative treatment of pancreatic cancer. Alternative or combined therapeutic options in particular consist of adjuvant or neoadjuvant chemotherapy, with or without radiotherapy. Palliative treatment for locally advanced disease may benefit patient's health status and quality of life. Limitations in healthcare resources, burden of treatment, and uncertainty of the net clinical benefit of adjuvant therapy, underline the need to identify the cost-effectiveness of different therapeutic approaches, as well as a need to establish patient groups who benefit most from these treatments. The present paper reviews cost-effectiveness studies published on pancreatic cancer treatment.

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[243]

TÍTULO / TITLE: - Enhancement effect of dihydroartemisinin on human gammadelta T cell proliferation and killing pancreatic cancer cells.

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

REVISTA / JOURNAL: - Int Immunopharmacol. 2013 Nov;17(3):850-7. doi: 10.1016/j.intimp.2013.09.015. Epub 2013 Oct 5.

●● Enlace al texto completo (gratuito o de pago) 1016/j.intimp.2013.09.015

AUTORES / AUTHORS: - Zhou ZH; Chen FX; Xu WR; Qian H; Sun LQ; Lu XT; Chen L; Zhang J; Ji HC; Fei SJ

INSTITUCIÓN / INSTITUTION: - Department of Central Laboratory, 97th Hospital of PLA, 226 Tongshan Road, Xuzhou 221004, Jiangsu, China. Electronic address: zhouzhonghai298@aliyun.com.

RESUMEN / SUMMARY: - gammadelta T cells play important roles in innate immunity against tumors and infections. Inhibitory effect of dihydroartemisinin on growth of cancer cells has been found in recent years. In this study, we investigated the effect of dihydroartemisinin on human gammadelta T cell proliferation by MTT assay and killing activity against pancreatic cancer cells SW1990, BxPC-3 and PANC-1 by LDH release assay in vitro. Intracellular molecule alterations were verified by flow cytometry. The results suggested that appropriate concentration of dihydroartemisinin favored the expansion of gammadelta T cells and enhanced gammadelta T cell mediated killing activity against pancreatic cancer cells. Up-regulation of intracellular perforin, granzyme B expression and IFN-gamma production may be the important mechanism of dihydroartemisinin on increased antitumor activity of gammadelta T cells.

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[244]

TÍTULO / TITLE: - Molecular characterization of patient-derived human pancreatic tumor xenograft models for preclinical and translational development of cancer therapeutics.

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

REVISTA / JOURNAL: - Neoplasia. 2013 Oct;15(10):1138-50.

AUTORES / AUTHORS: - Mattie M; Christensen A; Chang MS; Yeh W; Said S; Shostak Y; Capo L; Verlinsky A; An Z; Joseph I; Zhang Y; Kumar-Ganesan S; Morrison K; Stover D; Challita-Eid P

INSTITUCIÓN / INSTITUTION: - Agensys, Inc, Santa Monica, CA.

RESUMEN / SUMMARY: - Preclinical evaluation of novel cancer agents requires models that accurately reflect the biology and molecular characteristics of human tumors. Molecular profiles of eight pancreatic ductal adenocarcinoma patient tumors were compared to corresponding passages of xenografts obtained by grafting tumor fragments into immunocompromised mice. Molecular characterization was performed by copy number analysis, gene expression and microRNA microarrays, mutation analysis, short tandem repeat (STR) profiling, and immunohistochemistry. Xenografts were found to be highly representative of their respective tumors, with a high degree of genetic stability observed by STR profiling and mutation analysis. Copy number variation (CNV) profiles of early and late xenograft passages were similar, with recurrent losses on chromosomes 1p, 3p, 4q, 6, 8p, 9, 10, 11q, 12p, 15q, 17, 18, 20p, and 21 and gains on 1q, 5p, 8q, 11q, 12q, 13q, 19q, and 20q. Pearson correlations of gene expression profiles of tumors and xenograft passages were above 0.88 for all models. Gene expression patterns between early and late passage xenografts were highly stable for each individual model. Changes observed in xenograft passages largely corresponded to human stromal compartment genes and inflammatory processes. While some differences exist between the primary tumors and corresponding xenografts, the molecular profiles remain stable after extensive passaging. Evidence for stability in molecular characteristics after several rounds of passaging lends confidence to clinical relevance and allows for expansion of models to generate the requisite number of animals required for cohorts used in drug screening and development studies.

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[245]

TÍTULO / TITLE: - Induction of M2-macrophages by tumour cells and tumour growth promotion by M2-macrophages: a quid pro quo in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreatology. 2013 Sep-Oct;13(5):508-16. doi: 10.1016/j.pan.2013.06.010. Epub 2013 Jul 6.
●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.06.010
AUTORES / AUTHORS: - Partecke LI; Gunther C; Hagemann S; Jacobi C; Merkel M; Sendler M; van Rooijen N; Kading A; Nguyen Trung D; Lorenz E; Diedrich S; Weiss FU; Heidecke CD; von Bernstorff W
INSTITUCIÓN / INSTITUTION: - Department of General, Visceral, Thoracic and Vascular Surgery, University Medicine Greifswald, Ernst-Moritz-Arndt-University, Ferdinand Sauerbruchstrasse, 17475 Greifswald, Germany. Electronic address: partecke@uni-greifswald.de.
RESUMEN / SUMMARY: - INTRODUCTION: More effective therapies are required to improve survival of pancreatic cancer. Possible immunologic targets include tumour associated macrophages (TAMs), generally consisting of M1- and M2-macrophages. We have analysed the impact of TAMS on pancreatic cancer in a syngeneic orthotopic murine model. METHODS: 6606PDA murine pancreatic cancer cells were orthotopically injected into C57BL6 mice. Tumour growth was monitored using MRI. Macrophages were depleted by clodronate liposomes. Tumours including microvessel density were evaluated using immunohistochemistry, immunofluorescence and/or cytometric beads assays. Naive macrophages were generated employing peritoneal macrophages. In vitro experiments included culturing of macrophages in tumour supernatants as well as tumour cells cultured in macrophage supernatants using arginase as well as Griess assays. RESULTS: Clodronate treatment depleted macrophages by 80% in livers ($p = 0.0051$) and by 60% in pancreatic tumours ($p = 0.0169$). MRI revealed tumour growth inhibition from 221.8 mm(3) to 92.3 mm(3) ($p = 0.0216$). Micro vessel densities were decreased by 44% ($p = 0.0315$). Yet, MCP-1-, IL-4- and IL-10-levels within pancreatic tumours were unchanged. 6606PDA culture supernatants led to a shift from naive macrophages towards an M2-phenotype after a 36 h treatment ($p < 0.0001$), reducing M1-macrophages at the same time ($p < 0.037$). In vivo, M2-macrophages represented 85% of all TAMs ($p < 0.0001$). Finally, culture supernatants of M2-macrophages induced tumour growth in vitro by 63.2% ($p = 0.0034$). CONCLUSIONS: This quid pro quo of tumour cells and M2-macrophages could serve as a new target for future immunotherapies that interrupt tumour promoting activities of TAMs and change the iNOS-arginase balance towards their tumoricidal capacities.

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[246]
TÍTULO / TITLE: - Involvement of microRNA-181b in the gemcitabine resistance of pancreatic cancer cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreatology. 2013 Sep-Oct;13(5):517-23. doi: 10.1016/j.pan.2013.06.007. Epub 2013 Jun 28.
●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.06.007
AUTORES / AUTHORS: - Takiuchi D; Eguchi H; Nagano H; Iwagami Y; Tomimaru Y; Wada H; Kawamoto K; Kobayashi S; Marubashi S; Tanemura M; Mori M; Doki Y

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Graduate School of Medicine, Osaka University, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan.

RESUMEN / SUMMARY: - BACKGROUND/OBJECTIVES: MicroRNAs (miRs) have been shown to regulate the sensitivity to several chemotherapeutic agents in various types of cancers. MiR-181b is one of such regulators, yet its importance in pancreatic cancer is not determined so far. The aim of this study was to investigate the relationship between microRNA (miR)-181b expression and gemcitabine resistance in pancreatic cancer cells. METHODS: The effects of overexpression or knockdown of miR-181b on four pancreatic cancer cell lines exposed to gemcitabine were examined. The induction of apoptosis and the changes of the cylindromatosis (CYLD) protein were examined. Furthermore, the effect of small interference RNA for CYLD (siCYLD) on cell viability and the relationship between CYLD and nuclear factor kappa B (NF-kappaB) were investigated. RESULTS: The expression of miR-181b was higher in BxPC3, Panc1 and PSN1 cells compared with MiaPaCa2 cells. Pre-miR-181b transfection into MiaPaCa2 cells increased their gemcitabine resistance, whereas anti-miR-181b transfection into the other pancreatic cancer cell lines reduced their resistance to gemcitabine and led to the induction of apoptosis. The protein levels of CYLD were increased by anti-miR-181b in Panc1 and PSN1 cells. Inhibition of CYLD increased the NF-kappaB activity and gemcitabine resistance in Panc1 and PSN1 cells. CONCLUSIONS: The present study demonstrated that miR-181b was associated with the resistance of pancreatic cancer cells to gemcitabine, and verified that miR-181b enhances the activity of NF-kappaB by inhibiting CYLD, leading to the resistance to gemcitabine. Our results suggest that miR-181b is a potential target for decreasing gemcitabine resistance.

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[247]

TÍTULO / TITLE: - Nuclear Nrf2 expression is related to a poor survival in pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Pathol Res Pract. 2013 Oct 15. pii: S0344-0338(13)00310-5. doi: 10.1016/j.prp.2013.10.001.

●● Enlace al texto completo (gratuito o de pago) 1016/j.prp.2013.10.001

AUTORES / AUTHORS: - Soini Y; Eskelinen M; Juvonen P; Karja V; Haapasaari KM; Saarela A; Karihtala P

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Forensic Medicine, Institute of Clinical Medicine, Pathology and Forensic Medicine, School of Medicine, University of Eastern Finland, Cancer Center of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland. Electronic address: ylermi.soini@uef.fi.

RESUMEN / SUMMARY: - The aim of this study was to investigate the expression of Nrf2, sulfiredoxin and DJ1 in pancreatic cancer. The expression of Nrf2, sulfiredoxin and DJ1 was studied immunohistochemically in a large set of pancreatic adenocarcinomas consisting of 103 cases. Eighty six percent of the cases showed cytoplasmic Nrf2 and 24% nuclear Nrf2 positivity. Sulfiredoxin positivity was observed in 54% and DJ1 positivity in all cases. Nuclear Nrf2 positivity had an association with sulfiredoxin (p=0.019) and was associated with a poor survival (p=0.010). Stage IV tumors tended to have a more nuclear Nrf2 expression (p=0.080). DJ1 expression was more often found in well-differentiated tumors (p=0.012), and DJ1 expression was

associated with better survival (p=0.020). According to the results, nuclear Nrf2 expression predicts a worse survival in pancreatic adenocarcinoma, which is in keeping with its protection of cells against oxidative or xenobiotic stress. In accordance with Nrf2's regulation of the synthesis of sulfiredoxin, there was an association between them (p=0.019). DJ1 had no association with Nrf2, and its expression predicted a better survival of patients.

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[248]
TÍTULO / TITLE: - Nonfunctional Pancreatic Neuroendocrine Tumors <2 cm on Preoperative Imaging are Associated with a Low Incidence of Nodal Metastasis and an Excellent Overall Survival.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Dec;17(12):2105-13. doi: 10.1007/s11605-013-2360-9. Epub 2013 Oct 8.
●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2360-9
AUTORES / AUTHORS: - Toste PA; Kadera BE; Tatishchev SF; Dawson DW; Clerkin BM; Muthusamy R; Watson R; Tomlinson JS; Hines OJ; Reber HA; Donahue TR
INSTITUCIÓN / INSTITUTION: - Division of General Surgery, Department of Surgery, David Geffen School of Medicine at University of California, Los Angeles (UCLA), Los Angeles, CA, USA, ptoste@mednet.ucla.edu.
RESUMEN / SUMMARY: - BACKGROUND: The optimal surgical management of small nonfunctional pancreatic neuroendocrine tumors (NF-PNETs) remains controversial. We sought to identify (1) clinicopathologic factors associated with survival in NF-PNETs and (2) preoperative tumor characteristics that can be used to determine which lesions require resection and lymph node (LN) harvest. METHODS: The records of all 116 patients who underwent resection for NF-PNETs between 1989 and 2012 were reviewed retrospectively. Preoperative factors, operative data, pathology, surgical morbidity, and survival were analyzed. RESULTS: The overall 5- and 10-year survival rates were 83.9 and 72.8 %, respectively. Negative LNs (p = 0.005), G1 or G2 histology (p = 0.033), and age <60 years (p = 0.002) correlated with better survival on multivariate analysis. The 10-year survival rate was 86.6 % for LN-negative patients (n = 73) and 34.1 % for LN-positive patients (n = 32). Tumor size >/=2 cm on preoperative imaging predicted nodal positivity with a sensitivity of 93.8 %. Positive LNs were found in 38.5 % of tumors >/=2 cm compared to only 7.4 % of tumors <2 cm. CONCLUSIONS: LN status, a marker of systemic disease, was a highly significant predictor of survival in this series. Tumor size on preoperative imaging was predictive of nodal disease. Thus, it is reasonable to consider parenchyma-sparing resection or even close observation for NF-PNETs <2 cm.

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[249]
TÍTULO / TITLE: - Endoscopic therapy of necrotizing pancreatitis and pseudocysts.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Gastrointest Endosc Clin N Am. 2013 Oct;23(4):787-802. doi: 10.1016/j.giec.2013.06.013. Epub 2013 Aug 1.
●● Enlace al texto completo (gratuito o de pago) 1016/j.giec.2013.06.013
AUTORES / AUTHORS: - Fisher JM; Gardner TB

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology, Department of Medicine, University of Washington, 1959 Northeast Pacific Street, Box 356424, Seattle, WA 98195, USA.

RESUMEN / SUMMARY: - Endoscopic therapy has become an essential component in the management of postpancreatitis complications, such as infected and/or symptomatic pancreatic pseudocysts and walled-off necrosis. However, although there have been 2 recent randomized, controlled trials performed, a general lack of comparative effectiveness data regarding the timing, indications, and outcomes of these procedures has been a barrier to the development of practice standards for therapeutic endoscopists managing these issues. This article reviews the available data and expert consensus regarding indications for endoscopic intervention, timing of procedures, endoscopic technique, periprocedural considerations, and complications.

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[250]

TÍTULO / TITLE: - Prognostic significance of epidermal growth factor receptor overexpression in pancreas cancer and nodal metastasis.

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

REVISTA / JOURNAL: - ANZ J Surg. 2013 Sep 25. doi: 10.1111/ans.12399.

●● Enlace al texto completo (gratuito o de pago) 1111/ans.12399

AUTORES / AUTHORS: - Perini MV; Montagnini AL; Coudry R; Patzina R; Penteado S; Abdo EE; Diniz A; Jukemura J; da Cunha JE

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Surgical Division, University of Sao Paulo Medical School, Sao Paulo, Brazil.

RESUMEN / SUMMARY: - BACKGROUND: Identification of molecular markers in pancreatic adenocarcinoma (PA) has the potential to guide targeted therapy. The objective of this study is to determine the prognostic significance of epidermal growth factor receptor (EGFR) expression (membrane and cytoplasmic) in resected PA and its correlation with lymph node metastasis and survival. METHODS: EGFR overexpression was determined by immunohistochemistry, and the pattern of expression was compared between the primary tumour, adjacent normal pancreas and involved lymph nodes. RESULTS: A total of 88 patients had curative resection. No difference was found in mEGFR overexpression between tumoural and metastatic nodal tissues (P = 0.28). Median overall survival time was 22.9 months. Overall cumulative 1-, 3- and 5-year survival was 48%, 20% and 18%, respectively. In positive mEGFR tumour expression, survival was 46% at 1 year, 8% at 3 years and 0% at 5 years (P < 0.05). Univariate analysis showed that male gender, portal vein (PV) resection, perineural, lymphovascular and peri-pancreatic invasion, positive margins and positive mEGFR expression in tumour tissue had worse survival. Multivariate analysis showed that male gender, PV resection, vascular and perineural invasion remained independent predictors of poor survival. CONCLUSION: Positive mEGFR overexpression is associated with decreased survival; however, it is not an independent prognostic factor.

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[251]

TÍTULO / TITLE: - Serum sialic acid as a marker of pancreatic cancers.

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

REVISTA / JOURNAL: - Clin Lab. 2013;59(7-8):781-8.
AUTORES / AUTHORS: - Gruszewska E; Chrostek L; Cylwik B; Tobolczyk J; Szmitkowski M; Kuklinski A; Kedra B
INSTITUCIÓN / INSTITUTION: - Department of Biochemical Diagnostics, Medical University of Bialystok, Poland.
RESUMEN / SUMMARY: - BACKGROUND: The carbohydrate alterations in sialoglycoproteins and sialoglycolipids cause the high serum concentration of sialic acid in many types of cancers. The aim of this study was to evaluate the diagnostic accuracy of total sialic acid (TSA), lipid-bound sialic acid (LSA), and free sialic acid (FSA) in patients with primary pancreatic cancers. METHODS: TSA and LSA concentrations in the sera of 42 patients were measured by the enzymatic and FSA by the thiobarbituric method. RESULTS: The mean levels of TSA, LSA, and FSA in the sera of patients with pancreatic cancers were significantly higher than in controls. Taking into consideration the size and the location of the tumors, regional lymph node and distant metastases, there were no differences in TSA, FSA, and CA 19-9 levels. However, the location of tumors in the pancreas affects LSA levels. The sialic acids, contrary to CA 19-9, are not useful tools in the differential diagnosis of tumors and non-malignant diseases of the pancreas. LSA has the highest sensitivity, negative predictive value, accuracy, and the ability to discriminate cancer patients from healthy controls. The diagnostic power of LSA is similar to CA 19-9. CONCLUSIONS: We suggest that LSA can be useful in the diagnosis and evaluation of the tumor location in patients with primary pancreatic cancers.

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[252]
TÍTULO / TITLE: - Simvastatin delay progression of pancreatic intraepithelial neoplasia and cancer formation in a genetically engineered mouse model of pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreatology. 2013 Sep-Oct;13(5):502-7. doi: 10.1016/j.pan.2013.08.002. Epub 2013 Aug 20.
●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.08.002
AUTORES / AUTHORS: - Fendrich V; Sparn M; Lauth M; Knoop R; Plassmeier L; Bartsch DK; Waldmann J
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Philipps-University Marburg, Baldingerstrasse, D-35043 Marburg, Germany. Electronic address: fendrich@med.uni-marburg.de.
RESUMEN / SUMMARY: - BACKGROUND AND AIMS: Pancreatic cancer is among the most dismal of human malignancies. There are no chemopreventive strategies for pancreatic cancer or its precursor lesions, pancreatic intraepithelial neoplasia (PanINs). Recent evidence suggests that statins have potential chemopreventive abilities. In this study, we used a genetically engineered mouse model of pancreatic cancer to evaluate the chemopreventive potential of this drug. METHODS: Simvastatin was injected i.p. in LsL-Kras(G12D); Pdx1-Cre or LsL-Kras(G12D);LsL-Trp53(R172H);Pdx1-Cre mice. After five months, animals were sacrificed. The effect of simvastatin was evaluated by histopathological analyses, immunostaining, and real-time PCR. RESULTS: After five months of treatment, simvastatin was able to significantly delay progression of mPanINs in LsL-Kras(G12D); Pdx1-Cre mice. Furthermore, formation of invasive pancreatic cancer in LsL-Kras(G12D); LsL-Trp53(R172H); Pdx1-Cre transgenic mice

was partially inhibited by simvastatin. Invasive murine pancreatic cancer was identified in 9 of 12 (75%) LsL-Kras(G12D); LsL-Trp53(R172H);Pdx1-Cre untreated control mice. In contrast, transgenic mice treated with Simvastatin, only 4 out of 10 (40%, p = 0.004) developed murine pancreatic cancer during the study. Using real-time PCR we found a significant up-regulation of Hmgcr as sign of blocking HMG-CoA reductase, a key enzyme in the cholesterol biosynthesis. This shows our ability to achieve effective pharmacologic levels of simvastatin during pancreatic cancer formation in vivo. CONCLUSION: Using a transgenic mouse model that recapitulates human pancreatic cancer, this study provides first evidence that simvastatin is an effective chemopreventive agent by delaying the progression of PanINs and partially inhibit the formation of murine pancreatic cancer.

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[253]

TÍTULO / TITLE: - Radiographic Tumor-Vein Interface as a Predictor of Intraoperative, Pathologic, and Oncologic Outcomes in Resectable and Borderline Resectable Pancreatic Cancer.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Oct 16.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2374-3

AUTORES / AUTHORS: - Tran Cao HS; Balachandran A; Wang H; Nogueras-Gonzalez GM; Bailey CE; Lee JE; Pisters PW; Evans DB; Varadhachary G; Crane CH; Aloia TA; Vauthey JN; Fleming JB; Katz MH

INSTITUCIÓN / INSTITUTION: - Department of Surgical Oncology, The University of Texas M.D. Anderson Cancer Center, 1400 Pressler Street, FCT 17.6058, Houston, TX, 77230-1402, USA.

RESUMEN / SUMMARY: - BACKGROUND: Venous resection may be required to achieve complete resection of pancreatic cancers. We assessed the ability of radiographic criteria to predict the need for superior mesenteric-portal vein (SMV-PV) resection and the presence of histologic vein invasion. METHODS: All patients who underwent pancreaticoduodenectomy from 2004 to 2011 at the authors' institution were identified. Preoperative pancreatic protocol CT images were re-reviewed to characterize the extent of tumor-vein circumferential interface (TVI) as demonstrating no interface, </=180 degrees of vessel circumference, >180 degrees of vessel circumference, or occlusion. Findings were correlated with the need for venous resection, histologic venous invasion, and survival. RESULTS: A total of 254 patients underwent pancreaticoduodenectomy and met inclusion criteria; 98 (39.6 %) required SMV-PV resection. In our cohort, 76.4 % of patients received neoadjuvant chemoradiation. The TVI classification system predicted with fair accuracy both the need for SMV-PV resection at the time of surgery and histologic invasion of the vein. In particular, 89.5 % of patients with TVI >180 degrees or occlusion required SMV-PV resection. Of those, 82.4 % had documented histologic SMV-PV invasion. TVI </=180 degrees was associated with favorable overall survival compared to a greater circumferential interface. CONCLUSIONS: A tomographic classification of the tumor-SMV-PV interface can predict the need for venous resection, pathologic venous involvement, and survival. To assist in treatment planning, a standardized assessment of this anatomic relationship should be routinely performed.

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[254]

TÍTULO / TITLE: - Factors Predicting Long-Term Survival Following Pancreatic Resection for Ductal Adenocarcinoma of the Pancreas: 40 Years of Experience.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Nov 16.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2408-x

AUTORES / AUTHORS: - Dusch N; Weiss C; Strobel P; Kienle P; Post S; Niedergethmann M

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Faculty of Medicine Mannheim, University Medical Centre Mannheim, University of Heidelberg, 68167, Mannheim, Germany.

RESUMEN / SUMMARY: - BACKGROUND: Long-term survival after resection for pancreas carcinoma has rarely been reported. Factors influencing long-term survival are still under debate. The aim of this study was to define predictors for long-term survival. METHODS: Between 1972 and 2004, a total of 415 patients underwent resection. Data were collected in a prospective data base. Data of 360 patients were available for further analysis in 2011. All specimens of long-term survivors were histologically reviewed. RESULTS: Long-term survivors (n = 69) had a median survival of 91 months. Pathological re-evaluation of all specimens re-confirmed the diagnosis. Predictive factors for long-term survival in univariate analysis were no preoperative biliary stent, low CA 19-9 level, lack of blood transfusion, R0 resection, tumour diameter, and -grading, absence of lymph node or distant metastases, lymphangiosis, and perineural infiltration. Adjuvant chemotherapy showed a significant influence on overall survival but not on long-term survival. In multivariate analysis, lymph node ratio and volume of blood transfusion were predictors of long-term survival. CONCLUSION: Nearly 20 % of patients with pancreas carcinoma who undergo surgical resection have a chance of long-term survival. Survival beyond 5 years is predicted by clinical and tumour-specific factors. Adjuvant chemotherapy might prolong overall survival but is, according to these results, unable to contribute to long-term survival. There is still a risk of recurrence after a 5- or even a 12-year mark. Survival beyond 5 or even 12 years, therefore, does not assure cure.

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[255]

TÍTULO / TITLE: - Five-year actual survival after pancreatoduodenectomy for pancreatic head cancer.

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

REVISTA / JOURNAL: - ANZ J Surg. 2013 Oct 28. doi: 10.1111/ans.12422.

●● Enlace al texto completo (gratuito o de pago) 1111/ans.12422

AUTORES / AUTHORS: - Perysinakis I; Avlonitis S; Georgiadou D; Tsipras H; Margaris I

INSTITUCIÓN / INSTITUTION: - 3rd Surgical Department, George Gennimatas General Hospital of Athens, Athens, Greece.

RESUMEN / SUMMARY: - BACKGROUND: The aim of this study was to analyse retrospectively the long-term results of patients who were operated for adenocarcinoma of the pancreatic head and identify significant prognostic factors. METHODS: Eighty patients who were surgically treated for adenocarcinoma of the pancreatic head

between 1995 and 2006 met the inclusion criteria and were subject to retrospective analysis. Possible prognostic factors were evaluated and independent predictors of survival were determined. RESULTS: A classic Whipple procedure was performed in 47 patients and a pylorus-preserving pancreatoduodenectomy in 32 patients; one patient underwent total pancreatectomy. Five-year survival rate in this group of patients was 13.6%. Median survival time was 24 months. Univariable analysis demonstrated stage of disease, tumour size and grade and nodal status as significant predictive factors of survival. Multivariable analysis indicated tumour size, nodal status and disease stage as significant prognostic indicators in terms of survival. CONCLUSIONS: Long-term survival in pancreatic cancer is still very low. Prognostic factors include differentiation of the tumour, disease stage and nodal status. So far, there has been no reliable method that can accurately predict which patient will mostly benefit from surgical resection. This means that pancreatic cancer resection should nearly always be attempted.

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[256]

TÍTULO / TITLE: - B7H4, HSP27 and DJ-1 molecular markers as prognostic factors in pancreatic cancer.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Nov-Dec;13(6):564-9. doi: 10.1016/j.pan.2013.10.005. Epub 2013 Oct 23.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.10.005

AUTORES / AUTHORS: - Tsiaousidou A; Lambropoulou M; Chatzitheoklitos E; Tripsianis G; Tsompanidou C; Simopoulos C; Tsaroucha AK

INSTITUCIÓN / INSTITUTION: - Department of Surgery, General Hospital 'Agios Dimitrios', Thessaloniki, Greece; 2nd Department of Surgery and Laboratory of Experimental Surgery, Faculty of Medicine, Democritus University of Thrace, Alexandroupolis, Greece. Electronic address: natasha_tsia@yahoo.com.

RESUMEN / SUMMARY: - OBJECTIVES: Pancreatic cancer (PC) is one of the most lethal tumors of the gastrointestinal tract. The ability to predict which patients would benefit most from surgical intervention and chemotherapy would be a great clinical tool. A large number of potential markers have been identified lately in pancreatic cancer and their clinical utilities as prognostic tools are under investigation. METHODS: We recruited 41 patients who had undergone radical surgical resection for PC between 2003 and 2010. To investigate the prognostic factors, we evaluated 3 possible markers: B7H4, HSP27 and DJ-1 protein expressions in the tissue specimens of these 41 patients by immunohistochemistry and analyzed the clinical and pathological features of these specimens. RESULTS: The expression of the three antigens was independently associated with a negative impact of chemotherapy with gemcitabine on patient's survival. Moreover, patients who overexpressed B7H4 had worse prognosis than the ones who did not. CONCLUSIONS: B7H4, DJ-1 and HSP27 may be used in the future as prognostic markers that express resistance of pancreatic cancer patients to chemotherapy with gemcitabine.

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[257]

TÍTULO / TITLE: - MUC2 expression and prevalence of high-grade dysplasia and invasive carcinoma in mixed-type intraductal papillary mucinous neoplasm of the pancreas.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Nov-Dec;13(6):583-8. doi: 10.1016/j.pan.2013.08.007. Epub 2013 Aug 30.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.08.007

AUTORES / AUTHORS: - Masuda A; Arisaka Y; Hara S; Matsumoto I; Takenaka M; Sakai A; Shiomi H; Matsuki N; Sugimoto M; Fujita T; Hayakumo T; Ku Y; Ogino S; Azuma T; Kutsumi H

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology, Department of Internal Medicine, Graduate School of Medicine, Kobe University, 7-5-1, Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan.

RESUMEN / SUMMARY: - BACKGROUND/OBJECTIVES: Morphological types and mucin protein expressions classify intraductal papillary mucinous neoplasms (IPMNs). Main duct (MD)-IPMN mostly consists of intestinal type (I-type), which expresses MUC2. Branch duct (BD)-IPMN mostly consists of gastric type (G-type), which does not express MUC2. However, the definition of mixed-type IPMN has yet to be clarified and it contains various histological types. The aim of this study was to investigate the relationship between MUC2 expression and the presence of high-grade dysplasia (HGD) and invasive carcinoma, especially in mixed-type IPMN. METHODS: This retrospective study included 101 consecutive patients with surgically resected IPMNs between April 2001 and October 2012. All patients were morphologically classified into four distinct types (I-type, G-type, PB-type: pancreatobilliary, O-type: oncocytic) and immunohistochemical reactivity of various anti-mucin antibodies were investigated. RESULTS: According to the classification of the 2012 international guidelines, the numbers (and histomorphological types: I/G/PB/O) of MD, mixed-type, and BD-IPMNs were 16 (12/4/0/0), 45 (16/28/1/0), and 40 (0/38/1/1). Prevalence of MUC2 expression in MD, mixed-type, and BD-IPMNs were 75% (12/16), 36% (16/45), and 0% (0/40). In mixed-type IPMN, the prevalence of HGD and/or invasive carcinoma in MUC2-positive IPMN was significantly higher than that of MUC2-negative IPMN (HGD + invasive carcinoma: 88% vs. 38%, p = 0.0017; invasive carcinoma: 50% vs. 21%, p = 0.042). Multivariate analysis showed that MUC2 expression is an independent predictive factor of HGD and invasive carcinoma in mixed IPMN (odds ratio 14.6, 95% CI 2.5-87.4, p = 0.003). CONCLUSIONS: In mixed-type IPMN, MUC2 expression clearly identified HGD and invasive carcinoma and may provide most appropriate surgical indication.

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[258]

TÍTULO / TITLE: - Liver transplantation for nonresectable metastatic solid pseudopapillary pancreatic cancer.

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

REVISTA / JOURNAL: - Ann Transplant. 2013 Nov 27;18:651-3. doi: 10.12659/AOT.889979.

●● Enlace al texto completo (gratuito o de pago) 12659/AOT.889979

AUTORES / AUTHORS: - Lagiewska B; Pacholczyk M; Lisik W; Cichocki A; Nawrocki G; Trzebicki J; Chmura A

RESUMEN / SUMMARY: - Background: Solid pseudopapillary tumor (SPT) of the pancreas, also known as Franz tumor, Hamoudie tumor, solid-cystic-papillary epithelial neoplasm, or solid and cystic tumor, is a neoplasm of transitory (potential) malignancy, seen predominantly in young women. Case Report: This report presents a female patient treated for a solid pseudopapillary tumor of the pancreas with hepatic metastases. The tumor was first diagnosed in 2006. Non-specific abdominal pain was the first presenting symptom. The patient underwent distal pancreatic resection and splenectomy in July 2006. Multifocal metastatic disease seen at surgery precluded radical resection. Following definitive pathology confirmation and the exclusion of extrahepatic metastases, the patient was referred to our transplant centre 18 months after pancreatic surgery, to be considered for orthotopic liver transplantation (OLTx). The extent of the disease was once again evaluated by imaging studies, followed by exploratory laparotomy. The patient underwent cadaveric liver transplantation in March 2008, with triple immunosuppression (tacrolimus, MMF, and steroids) following surgery. Presently, more than 5 years post-transplant, the patient has no signs of recurrent neoplasmatic disease. Conclusions: This is the first liver transplantation for a metastatic pancreatic pseudopapillary tumor in Poland, with the longest follow-up period described in the literature. Follow-up suggests a cautiously optimistic prognosis despite primary unresectability of hepatic metastases and the necessity for immunosuppressive therapy.

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[259]

TÍTULO / TITLE: - Altered MENIN expression disrupts the MAFA differentiation pathway in insulinoma.

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

REVISTA / JOURNAL: - Endocr Relat Cancer. 2013 Oct 24;20(6):833-48. doi: 10.1530/ERC-13-0164. Print 2013 Dec.

●● Enlace al texto completo (gratuito o de pago) 1530/ERC-13-0164

AUTORES / AUTHORS: - Hamze Z; Vercherat C; Bernigaud-Lacheretz A; Bazzi W; Bonnavion R; Lu J; Calender A; Pouponnot C; Bertolino P; Roche C; Stein R; Scoazec JY; Zhang CX; Cordier-Bussat M

INSTITUCIÓN / INSTITUTION: - INSERM U1052/CNRS UMR5286/Universite de Lyon, Lyon1 UMR-S1052, Cancer Research Center of Lyon, Lyon F-69008, France Service de Genetique Moleculaire et Clinique, Hospices Civils de Lyon, Hopital Edouard Herriot, Lyon F-69437, France UMR 3347/CNRS, U1021/INSERM, Institut Curie, Orsay F-91405, France Service Central d'Anatomie et Cytologie Pathologiques, Hospices Civils de Lyon, Hopital Edouard Herriot, Lyon F-69437, France Department of Molecular Physiology and Biophysics, Vanderbilt University Medical Center, Nashville, Tennessee 37232, USA.

RESUMEN / SUMMARY: - The protein MENIN is the product of the multiple endocrine neoplasia type I (MEN1) gene. Altered MENIN expression is one of the few events that are clearly associated with foregut neuroendocrine tumours (NETs), classical oncogenes or tumour suppressors being not involved. One of the current challenges is to understand how alteration of MENIN expression contributes to the development of these tumours. We hypothesised that MENIN might regulate factors maintaining endocrine-differentiated functions. We chose the insulinoma model, a paradigmatic example of well-differentiated pancreatic NETs, to study whether MENIN interferes with

the expression of v-MAF musculoaponeurotic fibrosarcoma oncogene homologue A (MAFA), a master glucose-dependent transcription factor in differentiated beta-cells. Immunohistochemical analysis of a series of human insulinomas revealed a correlated decrease in both MENIN and MAFA. Decreased MAFA expression resulting from targeted Men1 ablation was also consistently observed in mouse insulinomas. In vitro analyses using insulinoma cell lines showed that MENIN regulated MAFA protein and mRNA levels, and bound to Mafa promoter sequences. MENIN knockdown concomitantly decreased mRNA expression of both Mafa and beta-cell differentiation markers (Ins1/2, Gck, Slc2a2 and Pdx1) and, in parallel, increased the proliferation rate of tumours as measured by bromodeoxyuridine incorporation. Interestingly, MAFA knockdown alone also increased proliferation rate but did not affect the expression of candidate proliferation genes regulated by MENIN. Finally, MENIN variants with missense mutations detected in patients with MEN1 lost the WT MENIN properties to regulate MAFA. Together, our findings unveil a previously unsuspected MENIN/MAFA connection regarding control of the beta-cell differentiation/proliferation balance, which could contribute to tumorigenesis.

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[260]

TÍTULO / TITLE: - Resection of Isolated Renal Cell Carcinoma Metastases of the Pancreas: Outcomes from the Johns Hopkins Hospital.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Oct 26.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2278-2

AUTORES / AUTHORS: - Tosoian JJ; Cameron JL; Allaf ME; Hruban RH; Nahime CB; Pawlik TM; Pierorazio PM; Reddy S; Wolfgang CL

INSTITUCIÓN / INSTITUTION: - The Department of Surgery, Johns Hopkins Medical Institutions Sol Goldman Pancreatic Research Center, 604 Blalock Building, 600 N. Wolfe Street, Baltimore, MD, 21287, USA.

RESUMEN / SUMMARY: - PURPOSE: This study aims to assess outcomes and characteristics associated with resection of metastatic renal cell carcinoma (mRCC) to the pancreas. MATERIALS AND METHODS: From April 1989 to July 2012, a total of 42 patients underwent resection of pancreatic mRCC at our institution. We retrospectively reviewed records from a prospectively managed database and analyzed patient demographics, comorbidities, perioperative outcomes, and overall survival. Cox proportional hazards models were used to evaluate the association between patient-specific factors and overall survival. RESULTS: The mean time from resection of the primary tumor to reoperation for pancreatic mRCC was 11.2 years (range, 0-28.0 years). In total, 17 patients underwent pancreaticoduodenectomy, 16 underwent distal pancreatectomy, and 9 underwent total pancreatectomy. Perioperative complications occurred in 18 (42.9 %) patients; there were two (4.8 %) perioperative mortalities. After pancreatic resection, the median follow-up was 7.0 years (0.1-23.2 years), and median survival was 5.5 years (range, 0.4-21.9). The overall 5-year survival was 51.8 %. On univariate analysis, vascular invasion (hazard ratio, 5.15; p = 0.005) was significantly associated with increased risk of death. CONCLUSIONS: Pancreatic resection of mRCC can be safely achieved in the majority of cases and is associated with long-term survival. Specific pathological factors may predict which patients will benefit most from resection.

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[261]

TÍTULO / TITLE: - Perioperative Outcomes of Pancreaticoduodenectomy Compared to Total Pancreatectomy for Neoplasia.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Oct 29.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2393-0

AUTORES / AUTHORS: - Bhayani NH; Miller JL; Ortenzi G; Kaifi JT; Kimchi ET; Staveley-O'Carroll KF; Gusani NJ

INSTITUCIÓN / INSTITUTION: - Department of Surgery, College of Medicine; Program for Liver, Pancreas, & Foregut Tumors, Penn State Cancer Institute, The Pennsylvania State University, 500 University Drive, H070, Hershey, PA, 17033-0850, USA.

RESUMEN / SUMMARY: - PURPOSE: Total pancreatectomy (TP) eliminates the risk and morbidity of pancreatic leak after pancreaticoduodenectomy (PD). However, TP is a more extensive procedure with guaranteed endocrine and exocrine insufficiency. Previous studies conflict on the net benefit of TP. METHODOLOGY: A comparison of patients undergoing non-emergent, curative-intent TP or PD for pancreatic neoplasia using the National Surgical Quality Improvement Project data from 2005-2011 was done. Main outcome measures were mortality and major and minor morbidities. RESULTS: Of the 6,314 (97 %) who underwent PD and the 198 (3 %) who underwent TP, malignancy was present in 84 % of patients. The two groups were comparable at baseline. Mortality was higher after TP (6.1 %) than DP (3.1 %), p = 0.02. Adjusting for differences on multivariable analysis, TP carried increased mortality (OR 2.64, 95 % CI 1.3-5.2, p = 0.005). TP was also associated with increased rates of major morbidity (38 vs. 30 %, p = 0.02) and blood transfusion (16 vs. 10 %, p = 0.01). Infectious and septic complications occurred equally in both groups. CONCLUSION: The morbidity of a pancreatic fistula can be eliminated by TP. However, based on our findings, TP is associated with increased major morbidity and mortality. TP cannot be routinely recommended for to reduce perioperative morbidity when pancreaticoduodenectomy is an appropriate surgical option.

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[262]

TÍTULO / TITLE: - The role of lymph node ratio in recurrence after curative surgery for pancreatic endocrine tumours.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Nov-Dec;13(6):589-93. doi: 10.1016/j.pan.2013.09.001. Epub 2013 Sep 19.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.09.001

AUTORES / AUTHORS: - Ricci C; Casadei R; Taffurelli G; Buscemi S; D'Ambra M; Monari F; Santini D; Campana D; Tomassetti P; Minni F

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Emergency and Surgery (DIMES), Alma Mater Studiorum, University of Bologna, S.Orsola-Malpighi Hospital, Italy. Electronic address: claudiochir@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: The prognostic role of lymph nodes metastasis in pancreatic neuroendocrine tumours is unclear. METHODS: Retrospective study of 53 patients who underwent a curative standard resection for pancreatic

neuroendocrine tumours. The endpoint was to define the role of the lymph nodes ratio in recurrence after curative surgery. The following data were considered as possible factors for predicting the risk of recurrence: gender, age, presence of symptoms, hormonal status, site of tumours, type of resection, size of the tumours, radical resection, pathological T, N and M stage, the Ki67 index, the number of lymph nodes harvested, the number of metastatic lymph nodes and the lymph node ratio. Recurrence rate and time of recurrence were evaluated. RESULTS: Twelve (26.4%) patients developed a recurrence with a median time of 42.8 (1-305) months. At multivariate analysis, the only factors related to recurrence were: size of lesions (HR 1.1, C.I. 95% 1.0-1.1, P = 0.011), Ki67 >/= 5% (HR 3.6, C.I. 95% 1.3-10, P = 0.014) and LNR > 0.07 (HR 5.2, C.I. 95% 1.1-25, P = 0.045). CONCLUSIONS: Our study confirmed that the lymph nodes ratio played an important role in the recurrence rate and suggested that a low number of metastatic lymph nodes reduced the disease free survival.

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[263]

TÍTULO / TITLE: - Factors affecting the yield of endoscopic transpapillary bile duct biopsy for the diagnosis of pancreatic head cancer.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Sep-Oct;13(5):524-9. doi: 10.1016/j.pan.2013.08.005. Epub 2013 Aug 28.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.08.005

AUTORES / AUTHORS: - Kimura H; Matsubayashi H; Sasaki K; Ito H; Hirosawa K; Uesaka K; Kanemoto H; Ono H

INSTITUCIÓN / INSTITUTION: - Division of Endoscopy, Shizuoka Cancer Center, Nagaizumi, Suntogun, Shizuoka 411-8777, Japan; Division of Pathology, Shizuoka Cancer Center, Nagaizumi, Suntogun, Shizuoka 411-8777, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Transpapillary biliary biopsy (TBB) is a simple endoscopic technique that can be performed during an initial biliary drainage session. This procedure has the potential to reduce the load of another tissue sampling in cases of pancreatic head cancer (PHC) with biliary stricture. The aim of this study is to identify factors associated with a positive outcome using TBB for PHC. METHODS: In total, 130 cases that underwent TBB for investigation of distal biliary stricture were included [62 cases of PHC, 36 cases of distal biliary cancer (DBC), and 32 cases of benign biliary stricture (BBS)]. Factors affecting the diagnostic efficiency of TBB were determined using univariate and multivariate logistic analyses. RESULTS: Cancer tissue was obtained in 31 cases (50%) of PHC and 33 cases (91.7%) of DBC. Multivariable analysis showed that >==10 mg/dl of serum bilirubin level (odds ratio [OR]: 5.58; 95% confidence interval [CI]: 1.29-28.20; P = 0.021) and >==3 tissue samplings (OR: 3.59; 95% CI: 1.02-14.27, P = 0.046) were independent factors affecting cancer-positive rate in cases of PHC. In >90% of resected cases of PHC, cancer involved the left side of the biliary mucosa and the range of cancer invasion (>==2/3 of circumference of biliary mucosa) was also a significant factor (P = 0.001). CONCLUSIONS: PHC showing high level of serum bilirubin (>10 mg/dl) and high circumferential proportion of bile duct invasion (>2/3 judging from MDCT) is a good indication for biliary biopsy. Targeting the left-side wall and >==3 tissue samplings will lead to the higher sensitivity.

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[264]

TÍTULO / TITLE: - Selective Disruption of Rb-Raf-1 Kinase Interaction Inhibits Pancreatic Adenocarcinoma Growth Irrespective of Gemcitabine Sensitivity.

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

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Nov 21.

●● Enlace al texto completo (gratuito o de pago) 1158/1535-7163.MCT-12-0719

AUTORES / AUTHORS: - Trevino JG; Verma M; Singh S; Pillai S; Zhang D; Pernazza D; Sebti SM; Lawrence NJ; Centeno BA; Chellappan SP

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of 1Tumor Biology, 2Drug Discovery, and 3Anatomic Pathology, H. Lee Moffitt Cancer Center & Research Institute, Tampa; and 4Department of Surgery, University of Florida-Gainesville, Gainesville, Florida.

RESUMEN / SUMMARY: - Inactivation of the retinoblastoma (Rb) tumor suppressor protein is widespread in human cancers. Inactivation of Rb is thought to be initiated by association with Raf-1 (C-Raf) kinase, and here we determined how RRD-251, a disruptor of the Rb-Raf-1 interaction, affects pancreatic tumor progression. Assessment of phospho-Rb levels in resected human pancreatic tumor specimens by immunohistochemistry (n = 95) showed that increased Rb phosphorylation correlated with increasing grade of resected human pancreatic adenocarcinomas (P = 0.0272), which correlated with reduced overall patient survival (P = 0.0186). To define the antitumor effects of RRD-251 (50 mumol/L), cell-cycle analyses, senescence, cell viability, cell migration, anchorage-independent growth, angiogenic tubule formation and invasion assays were conducted on gemcitabine-sensitive and -resistant pancreatic cancer cells. RRD-251 prevented S-phase entry, induced senescence and apoptosis, and inhibited anchorage-independent growth and invasion (P < 0.01). Drug efficacy on subcutaneous and orthotopic xenograft models was tested by intraperitoneal injections of RRD-251 (50 mg/kg) alone or in combination with gemcitabine (250 mg/kg). RRD-251 significantly reduced tumor growth in vivo accompanied by reduced Rb phosphorylation and lymph node and liver metastasis (P < 0.01). Combination of RRD-251 with gemcitabine showed cooperative effect on tumor growth (P < 0.01). In conclusion, disruption of the Rb-Raf-1 interaction significantly reduces the malignant properties of pancreatic cancer cells irrespective of their gemcitabine sensitivity. Selective targeting of Rb-Raf-1 interaction might be a promising strategy targeting pancreatic cancer. Mol Cancer Ther; 12(12); 1-13. ©2013 AACR.

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[265]

TÍTULO / TITLE: - Selective inhibition of pancreatic ductal adenocarcinoma cell growth by the mitotic MPS1 kinase inhibitor, NMS-P715.

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

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Nov 26.

●● Enlace al texto completo (gratuito o de pago) 1158/1535-7163.MCT-13-0324

AUTORES / AUTHORS: - Slee RB; Grimes BR; Bansal R; Gore J; Blackburn C; Brown L; Gasaway R; Jeong J; Victorino J; March KL; Colombo R; Herbert BS; Korc M
INSTITUCIÓN / INSTITUTION: - 1Medical and Molecular Genetics, Indiana University.
RESUMEN / SUMMARY: - Most solid tumors, including pancreatic ductal adenocarcinoma (PDAC), exhibit structural and numerical chromosome instability (CIN). While often implicated as a driver of tumor progression and drug resistance, CIN also reduces cell fitness and poses a vulnerability which can be exploited therapeutically. The spindle assembly checkpoint (SAC) ensures correct chromosome-microtubule attachment, thereby minimizing chromosome segregation errors. Many tumors exhibit up-regulation of SAC components such as MPS1, which may help contain CIN within survivable limits. Prior studies showed that MPS1 inhibition with the small molecule, NMS-P715, limits tumor growth in xenograft models. In cancer cell lines, NMS-P715 causes cell death associated with impaired SAC function and increased chromosome mis-segregation. While normal cells appeared more resistant, effects on stem cells, which are the dose-limiting toxicity of most chemotherapeutics, were not examined. Elevated expression of 70 genes (CIN70), including MPS1, provides a surrogate measure of CIN and predicts poor patient survival in multiple tumor types. Our new findings show that the degree of CIN70 up-regulation varies considerably among PDAC tumors, with higher CIN70 gene expression predictive of poor outcome. We identified a 25 gene subset (PDAC CIN25) whose over-expression was most strongly correlated with poor survival and included MPS1. In vitro, growth of human and murine PDAC cells is inhibited by NMS-P715 treatment, whereas adipose-derived human mesenchymal stem cells are relatively resistant and maintain chromosome stability upon exposure to NMS-P715. These studies suggest that NMS-P715 could have a favorable therapeutic index and warrant further investigation of MPS1 inhibition as a new PDAC treatment strategy.

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[266]
TÍTULO / TITLE: - Proteomic strategy for probing complementary lethality of kinase inhibitors against pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Proteomics. 2013 Oct 24. doi: 10.1002/pmic.201300248.
●● Enlace al texto completo (gratuito o de pago) 1002/pmic.201300248
AUTORES / AUTHORS: - Lee JG; McKinney KQ; Mougeot JL; Bonkovsky HL; Hwang SI
INSTITUCIÓN / INSTITUTION: - Proteomics and Mass Spectrometry Research Laboratory, Carolinas HealthCare System, Charlotte, NC, USA.
RESUMEN / SUMMARY: - In the present study, proteomic analysis was performed to discover combinational molecular targets for therapy and chemoresistance by comparing differential protein expression from Panc-1 cells treated with FDA-approved drugs such as sunitinib, imatinib mesylate, dasatinib, and PD184352. A total of 4041 proteins were identified in the combined data from all of the treatment groups by nano-electrospray ultra-performance LC and MS/MS analysis. Most of the proteins with significant changes are involved in apoptosis, cytoskeletal remodeling, and epithelial-to-mesenchymal transition. These processes are associated with increased chemoresistance and progression of pancreatic cancer. Among the differentially expressed proteins, heme oxygenase-1 (HO-1) was found in the sunitinib and imatinib

mesylate treatment groups, which possibly acts as a specific target for synthetic lethality in combinational treatment. HO-1 was found to play a key role in sensitizing the chemoresistant Panc-1 cell line to drug therapy. Viability was significantly decreased in Panc-1 cells cotreated with sunitinib and imatinib mesylate at low doses, compared to those treated with sunitinib or imatinib mesylate alone. The results suggest that induction of chemosensitization by manipulating specific molecular targets can potentiate synergistic chemotherapeutic effects at lower, better tolerated doses, and in turn reduce the toxicity of multidrug treatment of pancreatic cancer.

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[267]
TÍTULO / TITLE: - "A Debate: Is Surgical Intervention for Cystic Neoplasms of the Pancreas Being Overutilized"
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Oct 29.
●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2394-z
AUTORES / AUTHORS: - Lillemoe KD
INSTITUCIÓN / INSTITUTION: - Department of Surgery, The Massachusetts General Hospital, Boston, MA, USA, klillemoe@partners.org.

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[268]
TÍTULO / TITLE: - Is Surgical Intervention for Cystic Neoplasms of the Pancreas Being Underutilized?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Oct 30.
●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2396-x
AUTORES / AUTHORS: - Schmidt CM
INSTITUCIÓN / INSTITUTION: - Departments of Surgery, Biochemistry and Molecular Biology, IU Health Pancreatic Cyst and Cancer Early Detection Center, Indiana University School of Medicine, 980 W Walnut St R3- C522, Indianapolis, IN, 46202, USA, maxschmi@iupui.edu.

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[269]
TÍTULO / TITLE: - Computed tomography staging of pancreatic cancer: A validation study addressing interobserver agreement.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreatology. 2013 Nov-Dec;13(6):570-5. doi: 10.1016/j.pan.2013.09.004. Epub 2013 Oct 10.
●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.09.004
AUTORES / AUTHORS: - Loizou L; Albiin N; Ansorge C; Andersson M; Segersvard R; Leidner B; Sundin A; Lundell L; Kartalis N
INSTITUCIÓN / INSTITUTION: - Department of Clinical Science, Intervention and Technology at Karolinska Institutet, Division of Medical Imaging and Technology, 14186 Stockholm, Sweden; Department of Radiology, Karolinska University Hospital, Huddinge, 14186 Stockholm, Sweden.

RESUMEN / SUMMARY: - BACKGROUND/OBJECTIVES: Ductal adenocarcinoma in the head of the pancreas (PDAC) is usually unresectable at the time of diagnosis due to the involvement of the peripancreatic vessels. Various preoperative classification algorithms have been developed to describe the relationship of the tumor to these vessels, but most of them lack a surgically based approach. We present a CT-based classification algorithm for PDAC based on surgical resectability principles with a focus on interobserver variability. METHODS: Thirty patients with PDAC undergoing pancreaticoduodenectomy were examined by using a standard CT protocol. Nine radiologists, representing three different levels of expertise, evaluated the CT examinations and the tumors were classified into four categories (A-D) according to the proposed system. For the interobserver agreement, the Intraclass Correlation Coefficient (ICC) was estimated. RESULTS: The overall ICC was 0.94 and the ICCs among the trainees, experienced radiologists, and experts were 0.85, 0.76, and 0.92, respectively. All tumors classified as category A1 showed no signs of vascular invasion at surgery. In category A2, 40% of the tumors had corresponding infiltration and required resection of the superior mesenteric vein/portal vein (SMV/PV). One of two tumors in category B2 and two of three in category C required SMV/PV resection. All six patients in category D had both arterial and venous involvement. CONCLUSION: There is almost perfect agreement among radiologists with different levels of expertise in regards to the local staging of PDAC. For tumors in a more advanced preoperative category, an increased risk for vascular involvement was noticed at surgery.

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[270]

TÍTULO / TITLE: - Cyst fluid SPINK1 may help to differentiate benign and potentially malignant cystic pancreatic lesions.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Sep-Oct;13(5):530-3. doi: 10.1016/j.pan.2013.06.008. Epub 2013 Jul 3.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.06.008

AUTORES / AUTHORS: - Raty S; Sand J; Laukkarinen J; Vasama K; Bassi C; Salvia R; Nordback I

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology and Alimentary Tract Surgery, Finland; ARC-NET Research Center, University and Hospital Trust of Verona, Italy. Electronic address: sari.raty@pshp.fi.

RESUMEN / SUMMARY: - OBJECTIVE: Differential diagnosis between benign and potentially malignant cystic pancreatic lesions may be difficult. Previously we have compared cyst fluid serine protease inhibitor Kazal type I (SPINK1) with some traditionally used tumour markers (amylase, CEA, Ca19-9) and found that it may be a new promising maker in the differential diagnosis of cystic pancreatic lesions. In the present study, we focused on cyst fluid SPINK1 levels in benign and potentially malignant cystic pancreatic lesions. DESIGN: Sixty-one patients operated on for cystic pancreatic lesion in Tampere University Hospital, Finland and in Verona University Hospital, Italy, were included. Cyst fluid was aspirated during surgery, stored at -70 degrees C, and analysed with immunofluorometric assay for SPINK1. The final diagnosis was acute pancreatitis with fluid collection (Acute FC) in 4 patients, chronic pseudocyst (PS) in 17 patients, serous cystadenoma (SCA) in 7 patients, mucinous cystadenoma (MCA) in 21 patients and intraductal papillary-mucinous neoplasm

(IPMN) in 12 patients (9 main/mixed duct type and 3 branch duct type). RESULTS: The acute FC patients had high SPINK1 levels. Among chronic cysts, SPINK1 levels were significantly higher in patients with potentially malignant cysts (main/mixed duct IPMN and MCA) than with benign cysts (side branch IPMN and SCA), (median and range, [480 (13-3602) vs. 18 (0.1-278) mug/L]; p < 0.0001). In the subcohort of 24 patients with <3 cm chronic cyst, cyst fluid SPINK 1 levels were significantly lower in SCA or side branch IPMN (3 [2-116] mug/L) than in main duct IPMN or MCA (638 [66-3602] mug/L; p = 0.018). The best sensitivity and specificity to differentiate any size MCA or main/mixed type IPMN from SCA or side branch IPMN were 85% and 84% (AUC 0.94; cut-off value 118 mug/L). The best sensitivity and specificity to differentiate <3 cm MCA or main duct IPMN from SCA or side branch IPMN were 93% and 89% (AUC 0.98; cut-off value 146 mug/L). CONCLUSIONS: Cyst fluid SPINK1 may be a possible marker in the differential diagnosis of benign and potentially malignant cystic pancreatic lesions.

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[271]

TÍTULO / TITLE: - Response to MLN8237 in pancreatic cancer is not dependent on RalA phosphorylation.

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

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Nov 12.

●● Enlace al texto completo (gratuito o de pago) 1158/1535-7163.MCT-12-1232

AUTORES / AUTHORS: - Neel NF; Stratford JK; Shinde V; Ecsedy JA; Martin TD; Der CJ; Yeh JJ

INSTITUCIÓN / INSTITUTION: - 1Lineberger Comprehensive Cancer Center1, The University of North Carolina at Chapel Hill.

RESUMEN / SUMMARY: - The high prevalence of KRAS mutations and importance of the RalGEF-Ral pathway downstream of activated K-Ras in pancreatic ductal adenocarcinoma (PDAC) emphasize the importance of identifying novel methods by which to therapeutically target these pathways. It was recently demonstrated that phosphorylation of RalA S194 by Aurora A kinase is critical for PDAC tumorigenesis. We sought to evaluate the Aurora A kinase-selective inhibitor MLN8237 as a potential indirect anti-RalA targeted therapy for PDAC. We utilized a site-specific phospho-S194 RalA antibody and determined that RalA S194 phosphorylation levels were elevated in a subset of PDAC cell lines and human tumors relative to unmatched normal controls. Effects of MLN8237 on anchorage-independent growth in PDAC cell lines and growth of patient-derived xenografts (PDX) were variable, with a subset of cell lines and PDX showing sensitivity. Surprisingly, RalA S194 phosphorylation levels in PDAC cell lines or PDX tumors did not correlate with MLN8237 responsiveness. However, we identified Ki67 as a possible early predictive biomarker for response to MLN8237 in PDAC. These results indicate that MLN8237 treatment may be effective for a subset of PDAC patients independent of RalA S194 phosphorylation. Ki67 may be an effective pharmacodynamic biomarker to identify response early in the course of treatment.

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[272]

TÍTULO / TITLE: - Depression, cytokines, and pancreatic cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Psychooncology. 2013 Oct 18. doi: 10.1002/pon.3422.
●● Enlace al texto completo (gratuito o de pago) 1002/pon.3422
AUTORES / AUTHORS: - Breitbart W; Rosenfeld B; Tobias K; Pessin H; Ku GY; Yuan J; Wolchok J
INSTITUCIÓN / INSTITUTION: - Psychiatry and Behavioral Sciences, Memorial Sloan Kettering Cancer Center, New York, NY, USA.
RESUMEN / SUMMARY: - BACKGROUND: The aim of this study was to examine the relationships between cytokines, depression, and pancreatic cancer. METHOD: A total of 75 individuals were recruited from two New York City hospitals (a cancer center and a psychiatric hospital) and composed of four subgroups: patients with adenocarcinoma of the pancreas who did (n = 17) and did not (n = 26) have a diagnosis of Major Depressive Episode (MDE), and healthy participants with (n = 7) and without (n = 25) MDE. All individuals completed a battery of self-report measures. Sera was assayed using Meso Scale Discovery techniques to measure the following pro-inflammatory and anti-inflammatory cytokines: IL-1beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-10, IL-12p70, IFN-gamma, TGF-beta, and TNF-alpha; we also calculated the IL-2/IL-4 ratio. RESULTS: Pancreatic cancer patients had significantly higher levels of IL-6 and IL-10 and significantly lower TGF-beta levels than healthy participants. When the sample was divided into those with and without MDE, the groups only differed with regard to serum IL-6 levels. No significant cancer and depression interaction effect was observed. Severity of depressive symptoms was also significantly correlated with IL-6, rs = 0.28 and p = 0.02, whereas hopelessness was associated with IFN-alpha, rs = 0.34 and p = 0.006. Pain, fatigue, and sleep disturbance were associated with several of the cytokines assayed including IL-1beta (pain intensity), IL-4 (pain intensity and overall sleep quality), IL-12p70 (pain intensity), and TGF-beta (fatigue intensity), but anxiety was not associated with any of the cytokines assayed. CONCLUSIONS: This study demonstrated an association between depression and IL-6, but not with other cytokines. Moreover, IL-6 was not significantly associated with other measures of psychological distress (anxiety and hopelessness) or with symptom distress (pain, fatigue, and sleep quality), although some cytokines assayed were associated with specific symptoms. The implications of these findings for the etiology and treatment of depression in pancreatic cancer patients are discussed. Copyright © 2013 John Wiley & Sons, Ltd.

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[273]
TÍTULO / TITLE: - Operative Resection is Currently Overutilized for Cystic Lesions of the Pancreas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Oct 29.
●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2395-y
AUTORES / AUTHORS: - Allen PJ
INSTITUCIÓN / INSTITUTION: - Hepatopancreatobiliary Service, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY, 10021, USA, ALLENP@MSKCC.ORG.

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[274]
TÍTULO / TITLE: - CA125 is Superior to CA19-9 in Predicting the Resectability of Pancreatic Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Dec;17(12):2092-8. doi: 10.1007/s11605-013-2389-9. Epub 2013 Oct 22.
●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2389-9
AUTORES / AUTHORS: - Luo G; Xiao Z; Long J; Liu Z; Liu L; Liu C; Xu J; Ni Q; Yu X
INSTITUCIÓN / INSTITUTION: - Pancreatic Cancer Institute, Fudan University, No. 270, Dong'An Road, Xuhui District, Shanghai, 200032, China.
RESUMEN / SUMMARY: - BACKGROUND: Although carbohydrate antigen 19-9 (CA19-9) has been reported as a biomarker to predict the resectability of pancreatic cancer, several limitations have restricted its clinical use. METHODS: The potential of several serum tumor markers (CA19-9, CA125, CA50, CA242, CA724, carcinoembryonic antigen (CEA), and alpha-fetoprotein (AFP)) to predict the resectability of pancreatic cancer was evaluated by receiver operating characteristic (ROC) analysis in a series of 212 patients with proven pancreatic cancer. RESULTS: Compared with other tumor markers including CA19-9, CA125 has a superior predictive value (CA19-9, ROC area 0.66, cutoff value 289.40 U/mL; CA125, ROC area 0.81, cutoff value 19.70 U/mL). In addition, for patients with unresectable diseases misjudged by CT as resectable, the percentage of CA125 over selected cutoff value was higher than that of CA19-9 (CA19-9, 70.27 %; CA125, 81.08 %). CONCLUSION: CA125 is superior to CA19-9 in predicting the resectability of pancreatic cancer. Aberrant high levels of CA125 may indicate unresectable pancreatic cancer.

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[275]
TÍTULO / TITLE: - Pancreatic pseudocyst simulating a pseudoaneurysm on Doppler sonography.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Ultrasound Q. 2013 Dec;29(4):329-31. doi: 10.1097/RUQ.0b013e3182a44ded.
●● Enlace al texto completo (gratuito o de pago)
1097/RUQ.0b013e3182a44ded
AUTORES / AUTHORS: - Momtahen AJ; Middleton WD; Teefey S; Duncan JR
INSTITUCIÓN / INSTITUTION: - Mallinckrodt Institute of Radiology, Washington University, St Louis, MO.
RESUMEN / SUMMARY: - Pancreatitis is associated with a wide variety of complications. Peripancreatic fluid collections and pseudoaneurysms are among the known complications of the disease. Doppler ultrasound is used in the evaluation of peripancreatic fluid collections to avoid misinterpretation of an aneurysm or a pseudoaneurysm as a simple or complex fluid collection. We report a case of recurrent pancreatitis complicated by peripancreatic fluid collection that mimicked a pseudoaneurysm.

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[276]
TÍTULO / TITLE: - Approach to cystic lesions of the pancreas.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Wien Med Wochenschr. 2013 Nov 20.
●● Enlace al texto completo (gratuito o de pago) 1007/s10354-013-0244-y
AUTORES / AUTHORS: - Schmid RM; Siveke JT
INSTITUCIÓN / INSTITUTION: - II. Medizinische Klinik, Klinikum rechts der Isar, Technische Universitat Munchen, Ismaningerstr. 22, 81675, Munchen, Deutschland, roland.schmid@lrz.tum.de.
RESUMEN / SUMMARY: - Cystic lesions of the pancreas are detected more frequently due to the improvement of imaging technologies. Their prevalence increases with age. In 95 % of cases, the spectrum of cystic neoplasia includes intraductal papillary mucinous neoplasia (IPMN), mucinous cystic neoplasia (MCN), serous cystic neoplasia, and solid pseudopapillary neoplasia (SPN). Diagnostic procedures aim to distinguish between neoplastic cystic and non-neoplastic cystic lesions as well as serous and mucinous lesions because of their different malignant potential. In most cases,cystic lesions are detected incidentally by computed tomography and magnetic resonance imaging (MRI) performed for other reasons. In our opinion, MRI/magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS) are complementary diagnostic procedures. In doubtful cases, cyst fluid analysis might be performed. The most frequent lesions are IPMNs. MRI/MRCP allows the detection of the number of cystic lesions, the relation to the main pancreatic duct, and the size of the lesion. EUS is superior to evaluate mural nodules. The relation to the main pancreatic duct can more easily appreciated with secretin MRI, MCN, SPN as well as main-duct type IPMN and BD-IPMN with “high-risk stigmata” for malignancy should be resected. Asymptomatic BD-IPMN without mural nodules, no main duct involvement, and a size less than 30 mm can be followed with a watchful waiting strategy.

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[277]
TÍTULO / TITLE: - Functional Modules Analysis Based on Coexpression Network in Pancreatic Ductal Adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pathol Oncol Res. 2013 Nov 2.
●● Enlace al texto completo (gratuito o de pago) 1007/s12253-013-9694-1
AUTORES / AUTHORS: - Shi B; Wang X; Han X; Liu P; Wei W; Li Y
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Tongji Hospital of Tongji University, Shanghai, China, shibaominsbm@hotmail.com.
RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is the most common epithelial, exocrine pancreatic malignancy, accounting for more than 80 % of the malignant neoplasms of the pancreas. Although the molecular basis of pancreatic cancer is now better understood than ever before, there remains a long distance from being completely understood. In this study, we identified the differentially expressed genes (DEGs) in PDAC tissue compared with normal tissue and constructed a co-expression network by computing the pairwise correlation coefficient between the DEGs. We applied a statistical approach of MCODE to cluster genes in the coexpression network. Ten functional modules were identified in this network. Our results strongly suggest that dysregulations of immune response, homeostasis and cell adhesion may significantly contribute to the development and progression of PDAC. Results from this study will provide the groundwork for the understanding of PDAC.

Future studies are needed to confirm some of the possible interactions suggested by this study.

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[278]

TÍTULO / TITLE: - Dilated papilla with mucin extrusion is a potential predictor of acute pancreatitis associated with intraductal papillary mucinous neoplasms of pancreas.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Nov-Dec;13(6):615-20. doi: 10.1016/j.pan.2013.09.003. Epub 2013 Sep 30.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.09.003

AUTORES / AUTHORS: - Hata T; Sakata N; Okada T; Aoki T; Motoi F; Katayose Y; Egawa S; Unno M

INSTITUCIÓN / INSTITUTION: - Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai, Miyagi 980-8574, Japan.

RESUMEN / SUMMARY: - BACKGROUND/OBJECTIVES: As intraductal papillary mucinous neoplasm (IPMN) of the pancreas is associated with acute pancreatitis (AP) in some cases, predicting the risk of pancreatitis is as important as predicting the risk of malignancy in IPMN cases. In this study, we attempted to clarify the characteristics of IPMN associated with AP, compared to those of IPMN not associated with AP. METHODS: From January 2006 to March 2013, data from 88 patients who underwent surgery for IPMN were retrospectively investigated and analyzed. We evaluated clinical and pathological variables of each patient and compared patients with IPMN with AP to those without AP. Furthermore, we presented representative cases of mild and severe pancreatitis caused by IPMN. RESULTS: Overall, 12 of 88 patients with IPMN (13.6%) had AP. Seven of the 12 patients had a single episode of AP, whereas the remaining 5 patients were diagnosed with IPMN with repeated AP. Ten of 12 patients with AP were diagnosed with mild AP and the remaining 2 with severe AP. Regarding clinical findings, the proportion of dilated papilla with mucin extrusion was significantly higher in patients with IPMN with AP than in those without AP ($p = 0.035$). Histological findings indicated that the proportion of intestinal-subtype IPMN was significantly higher in patients with IPMN with AP ($p = 0.013$). CONCLUSIONS: AP caused by IPMN derives mostly from intestinal IPMN. Dilated papilla with mucin extrusion can be a potential predictor of AP.

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[279]

TÍTULO / TITLE: - “Chronic” metastatic pancreatic acinar cell carcinoma.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Sep-Oct;13(5):549-52. doi: 10.1016/j.pan.2013.05.001. Epub 2013 May 10.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.05.001

AUTORES / AUTHORS: - Cananzi FC; Jayanth A; Lorenzi B; Belgaumkar A; Mochlinski K; Sharma A; Mudan S; Cunningham D

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The Royal Marsden, Fulham Road, London SW6 6JJ, UK. Electronic address: fcm.cananzi@hotmail.it.

RESUMEN / SUMMARY: - Acinar cell carcinoma (ACC) of the pancreas is a rare exocrine tumour for which there is very limited information about chemotherapy regimens and prognosis. Even though there are clinical guidelines for management of ductal cell carcinoma, a definitive and specific regime has not yet been agreed for this type of pancreatic cancer. We report a case of metastatic ACC of pancreas who has been treated with a multimodal approach, including novel combinations of different targeted drugs with conventional chemotherapy, surgery and radiofrequency ablation since the last 11 years. This degree of long term survival has not been reported so far in such a case of metastatic ACC of the pancreas. This case highlights the importance of a personalised multidisciplinary therapeutic strategy, employing locoregional therapies along with combinations of established and novel systemic therapies to control the disease, and the importance of flexibility when instigating new treatment paradigms for progressive cancer. Also, this case demonstrates that complete tumour eradication may not be the sole purpose of surgical oncology.

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[280]

TÍTULO / TITLE: - Retrospective Comparison of Robot-Assisted Minimally Invasive Versus Open Pancreaticoduodenectomy for Periampullary Neoplasms.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Nov 15.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2410-3

AUTORES / AUTHORS: - Bao PQ; Mazirka PO; Watkins KT

INSTITUCIÓN / INSTITUTION: - Stony Brook University Medical Center, HSC T-18, Room 065, Stony Brook, NY, 11794-8191, USA, philip.bao@stonybrook.edu.

RESUMEN / SUMMARY: - BACKGROUND: As with other open procedures now routinely performed using laparoscopy, minimally invasive pancreaticoduodenectomy (MIPD) may result in decreased pain, fewer wound complications, and accelerated recovery. However, when used for periampullary cancers, it is also important to assess if MIPD offers comparable oncologic outcomes. METHODS: Technical and perioperative outcomes were compared between patients with a preoperative diagnosis of periampullary neoplasm offered MIPD or open pancreaticoduodenectomy (OPD) from November 2009 to July 2011. RESULTS: Fifty-six consecutive MIPD and OPD (28 each) procedures were analyzed. Comparing MIPD to OPD, significant differences included longer median procedure time (431 vs 410 min, p = .04) and fewer median lymph nodes harvested (15 vs 20, p = .04). R0 resection rate tended to be lower (63 vs 88 %, p = .07) as well as surgical site infections (18 vs 43 %, p = .08). Clinically significant pancreatic fistula rate was the same between groups (21 %). Other outcomes such as narcotic pain medication use, length of stay, and 30-day readmission rates were also similar. CONCLUSIONS: MIPD is feasible with comparable technical success and outcomes to OPD. However, there is a learning curve to the procedure and further experience and prospective study will be required to better establish the oncologic efficacy of MIPD to open resection.

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[281]

TÍTULO / TITLE: - Activity of Drug-loaded Tumor-Penetrating Microparticles In Peritoneal Pancreatic Tumors.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Curr Cancer Drug Targets. 2013 Nov 4.
AUTORES / AUTHORS: - Lu Z; Tsai M; Wang J; Cole DJ; Wientjes MG; Au JL
INSTITUCIÓN / INSTITUTION: - Ze Lu, 9363 Towne Centre Drive, Suite 110, San Diego, CA 92121. zlu@optimumtx.com.
RESUMEN / SUMMARY: - Intraperitoneal (IP) chemotherapy confers significant survival benefits in cancer patients. However, several problems, including local toxicity and ineffectiveness against bulky tumors, have prohibited it from becoming a standard of care. We have developed drug-loaded, polymeric tumor-penetrating microparticles (TPM) to address these problems. Initial studies showed that TPM provides tumor-selective delivery and is effective against ovarian SKOV3 tumors of relatively small size (<50 mg). The present study evaluated whether the TPM activity extends to other tumor types that are more bulky and have different morphologies and disease presentation. We evaluated TPM in mice bearing two IP human pancreatic tumors with different growth characteristics and morphologies (rapidly growing, large and porous Hs766T vs. slowly growing, smaller and densely packed MiaPaCa2), and at different disease stage (early stage with smaller tumors vs. late stage with larger tumors plus peritoneal carcinomatosis). Comparison of treatments with TPM or paclitaxel in Cremophor micelles, at equi-toxic doses, shows, in all tumor types: (a) higher paclitaxel levels in tumors (up to 55-fold) for TPM, (b) greater efficacy for TPM, including significantly longer survival and higher cure rate, and (c) a single dose of TPM was equally efficacious as multiple doses of paclitaxel/Cremophor. The results indicate tumor targeting property and superior antitumor activity of paclitaxel-loaded TPM are generalizable to small and large peritoneal tumors, with or without accompanying carcinomatosis.

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[282]
TÍTULO / TITLE: - Palliation of pancreatic ductal obstruction in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Gastrointest Endosc Clin N Am. 2013 Oct;23(4):917-23. doi: 10.1016/j.giec.2013.06.010. Epub 2013 Aug 1.
●● Enlace al texto completo (gratuito o de pago) 1016/j.giec.2013.06.010
AUTORES / AUTHORS: - Sharaiha RZ; Widmer J; Kahaleh M
INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology & Hepatology, Department of Medicine, Weill Cornell Medical College, Street 1305 York Avenue, Fourth floor, New York, NY 10021, USA.
RESUMEN / SUMMARY: - Pancreatic stenting for patients with obstructive pain secondary to a malignant pancreatic duct stricture is safe and effective, and should be considered a therapeutic option. Although pancreatic stenting does not seem to be effective for patients with chronic pain, it may be beneficial in those with obstructive type pains, pancreatic duct disruption, or smoldering pancreatitis. Fully covered metal stents may be an option, but data on their use are limited. Further studies, including prospective randomized studies comparing plastic and metal stents in these indications, are needed to further validate and confirm these results.

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[283]

TÍTULO / TITLE: - Pseudotumor pancreatic tuberculosis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Tunis Med. 2013 Oct;91(10):623-4.
AUTORES / AUTHORS: - Ayadi S; Daghfous A; Maghrebi H; Belhadj A; Makni A; Rebai W; Bedioui H; Fteriche F; Ksantini R; Chebbi F; Jouini M; Kacem M; Ben Safta Z

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[284]
TÍTULO / TITLE: - Pancreatic metastasis from a solitary fibrous tumor of the kidney: A rare cause of acute recurrent pancreatitis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreatology. 2013 Nov-Dec;13(6):631-3. doi: 10.1016/j.pan.2013.06.004. Epub 2013 Jun 22.
●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.06.004
AUTORES / AUTHORS: - Patel YA; Dhalla S; Olson MT; Lennon AM; Khashab MA; Singh VK
INSTITUCIÓN / INSTITUTION: - Department of Medicine, Johns Hopkins Medical Institutions, Baltimore, MD, USA. Electronic address: ypatel2@jhmi.edu.
RESUMEN / SUMMARY: - Solitary fibrous tumors are unusual spindle cell neoplasms that uncommonly originate from the kidney. We report a case of a 43-year old male who presented with acute recurrent pancreatitis secondary to a mass in the head of the pancreas. Endoscopic ultrasound with fine needle aspiration (EUS-FNA) was performed. Cytology revealed solitary fibrous tumor of the kidney. This is the first reported case of solitary fibrous tumor metastasizing to the pancreas and presenting as acute recurrent pancreatitis.

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[285]
TÍTULO / TITLE: - Sorafenib does not improve efficacy of chemotherapy in advanced pancreatic cancer: A GISCAD randomized phase II study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Dig Liver Dis. 2013 Nov 1. pii: S1590-8658(13)00594-X. doi: 10.1016/j.dld.2013.09.020.
●● Enlace al texto completo (gratuito o de pago) 1016/j.dld.2013.09.020
AUTORES / AUTHORS: - Cascinu S; Berardi R; Sobrero A; Bidoli P; Labianca R; Siena S; Ferrari D; Barni S; Aitini E; Zagonel V; Caprioni F; Villa F; Mosconi S; Faloppi L; Tonini G; Boni C; Conte P; Di Costanzo F; Cinquini M
INSTITUCIÓN / INSTITUTION: - Medical Oncology Unit, Universita Politecnica delle Marche, Ospedali Riuniti di Ancona, Ancona, Italy. Electronic address: cascinu@yahoo.com.
RESUMEN / SUMMARY: - BACKGROUND: The RAF-MEK-ERK pathway is commonly activated in pancreatic cancer because of a high frequency of KRAS-BRAF mutations. A phase II randomized trial was designed to investigate the activity of sorafenib in combination with chemotherapy in advanced pancreatic cancer. METHODS: Locally advanced or metastatic pancreatic adenocarcinoma patients were randomized in a 1:1 ratio to receive cisplatin plus gemcitabine with sorafenib 400mg bid (arm A) or without sorafenib (arm B). RESULTS: One hundred and fourteen patients were enrolled; of these, 43 (74.6%) patients progressed in arm A and 44 (82.4%) in arm B. Median

progression-free survival was 4.3 months (95% CI: 2.7-6.5) and 4.5 months (95% CI: 2.5-5.2), respectively (HR=0.92; 95% CI: 0.62-1.35). Median overall survival was 7.5 (95% CI: 5.6-9.7) and 8.3 months (95% CI: 6.2-8.7), respectively (HR=0.95; 95% CI: 0.62-1.48). Response rates were 3.4% in arm A and 3.6% in arm B. CONCLUSIONS: Sorafenib does not significantly enhance activity of chemotherapy in advanced pancreatic cancer patients, and therefore should not be assessed in phase III trials.

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[286]

TÍTULO / TITLE: - Sequential gemcitabine and platinum versus first-line combination of gemcitabine and platinum for advanced pancreatic cancer treatment: a retrospective study.

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

REVISTA / JOURNAL: - Int J Clin Oncol. 2013 Sep 28.

●● Enlace al texto completo (gratuito o de pago) 1007/s10147-013-0622-x

AUTORES / AUTHORS: - Guo JC; Yang SH

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Yun-Lin Branch, National Taiwan University Hospital, Yunlin, Taiwan.

RESUMEN / SUMMARY: - OBJECTIVE: The purpose of this study was to investigate the impact of combinational versus sequential gemcitabine and platinum on prognosis of advanced pancreatic cancer. METHODS: Two hundred and three patients with advanced pancreatic cancer were selected. They were divided into GemP (first-line gemcitabine and platinum), Gem-then-P (sequential gemcitabine and platinum), Gem/other (first-line gemcitabine-based therapy without subsequent platinum), and Gem (first-line gemcitabine-based therapy without subsequent systemic therapy) groups. The Kaplan-Meier method and log-rank test were used for survival analyses. Cox regression model and propensity score matching were used for prognostic analyses. RESULTS: The median survival was 12.5 months [95 % confidence interval (CI), 11.2-13.7] in the GemP group (N = 65), 8.3 months (95 % CI 5.0-11.7) in the Gem-then-P group (N = 35), 11.6 months (95 % CI 4.6-18.5) in the Gem/other group (N = 26), and 4.7 months (95 % CI 3.3-6.0) in the Gem group (N = 77) (P < 0.001). Considering the GemP and Gem-then-P groups, performance status, serum creatinine, and response to first-line treatment were independent prognostic factors for overall survival in the multivariate analysis. No specific factors were identified for predicting the choice between GemP and Gem-then-P. CONCLUSIONS: First-line gemcitabine and platinum-based combinations were not superior to sequential gemcitabine and platinum for overall survival. The best sequence of chemotherapy for advanced pancreatic cancer should be explored in future clinical trials.

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[287]

TÍTULO / TITLE: - Clinical Significance and Revisiting the Meaning of CA 19-9 Blood Level Before and After the Treatment of Pancreatic Ductal Adenocarcinoma: Analysis of 1,446 Patients from the Pancreatic Cancer Cohort in a Single Institution.

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

REVISTA / JOURNAL: - PLoS One. 2013 Nov 8;8(11):e78977. doi: 10.1371/journal.pone.0078977.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0078977

AUTORES / AUTHORS: - Park JK; Paik WH; Ryu JK; Kim YT; Kim YJ; Kim J; Song BJ; Park JM; Yoon YB

INSTITUCIÓN / INSTITUTION: - Departments of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - BACKGROUND: Life expectancy of pancreatic ductal adenocarcinoma (PDAC) patients is usually short and selection of the most appropriate treatment is crucial. The aim of this study was to investigate the usefulness of serum CA 19-9 as a surrogate marker under no impress excluding other factors affecting CA 19-9 level other than tumor itself. METHODS: We recruited 1,446 patients with PDACs and patients with Lewis antigen both negative or obstructive jaundice were excluded to eliminate the false effects on CA 19-9 level. The clinicopathologic factors were reviewed including initial and post-treatment CA 19-9, and statistical analysis was done to evaluate the association of clinicopathologic factors with overall survival (OS). RESULTS: The total of 944 patients was enrolled, and205 patients (22%) underwent operation with curative intention and 541 patients (57%) received chemotherapy and/or radiotherapy. The median CA 19-9 levels of initial and post-treatment were 670 IU/ml and 147 IU/ml respectively. The prognostic factors affecting OS were performance status, AJCC stage and post-treatment CA 19-9 level in multivariate analysis. Subgroup analysis was done for the patients who underwent R0 and R1 resection, and patients with normalized post-operative CA 19-9 (</=37 IU/mL) had significantly longer OS and DFS regardless of initial CA 19-9 level; 32 vs. 18 months, P<0.001, 16 vs. 9 months, P = 0.004 respectively. CONCLUSIONS: Post-treatment CA 19-9 and normalized post-operative CA 19-9 (R0 and R1 resected tumors) were independent factors associated with OS and DFS, however, initial CA 19-9 level was not statistically significant in multivariate analysis.

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[288]

TÍTULO / TITLE: - RABL6A Promotes Oxaliplatin Resistance in Tumor Cells and Is a New Marker of Survival for Resected Pancreatic Ductal Adenocarcinoma Patients.

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

REVISTA / JOURNAL: - Genes Cancer. 2013 Jul;4(7-8):273-84. doi: 10.1177/1947601913501074.

- ●● Enlace al texto completo (gratuito o de pago) 1177 1947601913501074 [pii
- ●● Enlace al texto completo (gratuito o de pago) 1177/1947601913501074

AUTORES / AUTHORS: - Muniz VP; Askeland RW; Zhang X; Reed SM; Tompkins VS; Hagen J; McDowell BD; Button A; Smith BJ; Weydert JA; Mezhir JJ; Quelle DE

INSTITUCIÓN / INSTITUTION: - The Molecular and Cellular Biology Graduate Program, University of Iowa, Iowa City, IA, USA.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is characterized by early recurrence following pancreatectomy, rapid progression, and chemoresistance. Novel prognostic and predictive biomarkers are urgently needed to both stratify patients for clinical trials and select patients for adjuvant therapy regimens. This study sought to determine the biological significance of RABL6A (RAB, member RAS oncogene family-like protein 6 isoform A), a novel pancreatic protein, in PDAC. Analyses of RABL6A protein expression in PDAC specimens from 73 patients who underwent pancreatic resection showed that RABL6A levels are altered in 74% of tumors relative to adjacent benign ductal epithelium. Undetectable RABL6A expression, found in 7% (5/73) of patients, correlated with improved overall survival

(range 41 to 118 months with 3/5 patients still living), while patients with RABL6A expression had a worse outcome (range 3.3 to 100 months, median survival 20.3 months) (P = 0.0134). In agreement with those findings, RABL6A expression was increased in pancreatic cancer cell lines compared to normal pancreatic epithelial cells, and its knockdown inhibited pancreatic cancer cell proliferation and induced apoptosis. Moreover, RABL6A depletion selectively sensitized cells to oxaliplatin-induced arrest and death. This work reveals that RABL6A promotes the proliferation, survival, and oxaliplatin resistance of PDAC cells, whereas its loss is associated with extended survival in patients with resected PDAC. Such data suggest RABL6A is a novel biomarker of PDAC and potential target for anticancer therapy.

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[289]

TÍTULO / TITLE: - U.s. Food and drug administration approves Paclitaxel protein-bound particles (abraxane®) in combination with gemcitabine as first-line treatment of patients with metastatic pancreatic cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):686-8. doi: 10.6092/1590-8577/2028.

AUTORES / AUTHORS: - Saif MW

INSTITUCIÓN / INSTITUTION: - Tufts University School of Medicine. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

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[290]

TÍTULO / TITLE: - Healthcare costs, treatment patterns, and resource utilization among pancreatic cancer patients in a managed care population.

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

REVISTA / JOURNAL: - J Med Econ. 2013 Dec;16(12):1379-86. doi: 10.3111/13696998.2013.848208. Epub 2013 Oct 18.

●● Enlace al texto completo (gratuito o de pago) 3111/13696998.2013.848208

AUTORES / AUTHORS: - Dacosta Byfield S; Nash Smyth E; Mytelka D; Bowman L; Teitelbaum A

INSTITUCIÓN / INSTITUTION: - OptumInsight , Eden Prairie, MN , USA.

RESUMEN / SUMMARY: - Abstract Background: Pancreatic adenocarcinoma has few effective treatment options and poor survival. The objective of this study was to characterize treatment patterns and estimate the costs and resource use associated with its treatment in a commercially-insured US population. Methods: In this retrospective claims-based analysis, individuals >/=18 years old with evidence of pancreatic adenocarcinoma between January 1, 2001 and December 31, 2010 were selected from a managed care database. Treatment phase (either initial non-metastatic or metastatic) was determined using a claims-based algorithm. Patients in the pancreatic cancer population were matched 1:3 to a control population. Resource use (events/person-years), treatment patterns, and healthcare costs (per-patient per-month, PPPM) were determined during a variable length follow-up period (from first pancreatic cancer diagnosis to earliest of death, disenrollment, or study end). Results: In this study, 5262 pancreatic cancer patients were matched to 15,786 controls. Rates of office visits, inpatient visits, ER visits, and inpatient stays, and mean total all-cause healthcare costs PPPM ($15,480 vs $1001) were significantly higher among cancer patients than controls (all p < 0.001). Mean inpatient costs were the single largest cost driver ($9917 PPPM). Also, mean total all-cause healthcare costs were significantly

higher during the metastatic treatment phase vs the initial treatment phase of non-metastatic disease ($21,637 vs $10,358, p < 0.001). Conclusions: These results indicate that pancreatic cancer imposes a substantial burden on the US healthcare system, and that treatment of more advanced disease is significantly more costly than initial treatment of non-metastatic disease. Limitations: Additional research is needed to validate the accuracy of the claims-based algorithms used to identify the treatment phase.

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[291]

TÍTULO / TITLE: - Influence of perineural invasion on survival and recurrence in patients with resected pancreatic cancer.

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

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5133-9.

AUTORES / AUTHORS: - Zhang JF; Hua R; Sun YW; Liu W; Huo YM; Liu DJ; Li J

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China E-mail : lordhuarong@sohu.com.

RESUMEN / SUMMARY: - Background: Perineural invasion (PNI) has been reported as one of the sources of locoregional recurrence in resected pancreatic cancer (PC). However the impact of PNI in resected pancreatic cancer remains controversial. The purpose of this study was to determine the association between PNI status and clinical outcomes. Methods: Publications were identified which assessed prognostic significance of PNI status in resected pancreatic cancer up to February 2013. A meta-analysis was performed to clarify the association between PNI status and clinical outcomes. Results: A total of 21 studies met the inclusion criteria, covering 4,459 cases. Analysis of these data showed that intrapancreatic PNI was correlated with reduced overall survival only in resected pancreatic ductal adenocarcinoma (PDAC) patients (HR=1.982, 95%CI: 1.526-2.574, p=0.000). Extrapancreatic PNI was correlated with reduced overall survival in all resected pancreatic cancer patients (HR=1.748, 95%CI: 1.372- 2.228, p=0.000). Moreover, intrapancreatic PNI status may be associated with tumor recurrence in all resected pancreatic cancer patients (HR=2.714, 95%CI: 1.885-3.906, p=0.000). Conclusion: PNI was an independent and poor prognostic factor in resected PDAC patients. Moreover, intrapancreatic PNI status may be associated with tumor recurrence.

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[292]

TÍTULO / TITLE: - Prognostic value of 18F-fluorodeoxyglucose positron emission tomography in patients with resectable pancreatic cancer.

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

REVISTA / JOURNAL: - Yonsei Med J. 2013 Nov;54(6):1377-83. doi: 10.3349/ymj.2013.54.6.1377.

●● Enlace al texto completo (gratuito o de pago) 3349/ymj.2013.54.6.1377

AUTORES / AUTHORS: - Choi HJ; Kang CM; Lee WJ; Song SY; Cho A; Yun M; Lee JD; Kim JH; Lee JH

INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea. docnuke@yuhs.ac.

RESUMEN / SUMMARY: - PURPOSE: We evaluated the prognostic value of (18)F-2-fluoro-2-deoxyglucose positron emission tomography (FDG PET) in patients with resectable pancreatic cancer. MATERIALS AND METHODS: We retrospectively reviewed the medical records of pancreatic cancer patients who underwent curative resection, which included 64 consecutive patients who had preoperative FDG PET scans. For statistical analysis, the maximal standardized uptake value (SUVmax) of primary pancreatic cancer was measured. Survival time was estimated by the Kaplan-Meier method, and Cox's proportional hazard model was used to determine whether SUVmax added new predictive information concerning survival together with known prognostic factors. $p<0.05$ indicated statistical significance. RESULTS: Overall survival (OS) and disease- free survival (DFS) were respectively 42.9 months (27.6-58.2; 95% CI) and 14.9 months (10.1-19.7; 95% CI). When subjects were divided into two groups according to SUVmax with a cutoff value of 3.5, the high SUVmax group (n=32; SUVmax >3.5) showed significantly shorter OS and DFS than the low SUVmax group. Multivariate analysis of OS and DFS showed that both high SUVmax and poor tumor differentiation were independent poor prognostic factors. CONCLUSION: Our study showed that degree of FDG uptake was an independent prognostic factor in pancreatic cancer patients who underwent curative resection.

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[293]

TÍTULO / TITLE: - The incidence and survival rate of population-based pancreatic cancer patients: shanghai cancer registry 2004-2009.

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

REVISTA / JOURNAL: - PLoS One. 2013 Oct 9;8(10):e76052. doi: 10.1371/journal.pone.0076052.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0076052

AUTORES / AUTHORS: - Luo J; Xiao L; Wu C; Zheng Y; Zhao N

INSTITUCIÓN / INSTITUTION: - Department of Health Statistics and Social Medicine, School of Public Health, Fudan University, Shanghai, China.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is a devastating disease with dismal prognosis. Large population-based evidence on its survival rate and influence factors is lacking in China. OBJECTIVE: This study aimed to depict the demographic factors, tumor characteristics, incidence rate and survival rate of pancreatic cancer cases in urban China. METHODS: The demographic factors, tumor characteristics were collected for all the pancreatic cancer cases identified during 2004 to 2009 from the Shanghai Cancer Registry. The survival time was ascertained through linkage of the Shanghai Cancer Registry and the Shanghai Vital Statistics Registry. The deadline of death certificates was the end of December 2012. Kaplan-Meier method and Cox proportional-hazards regression model were used to explore the survival rate and influence factors. RESULTS: 11,672 new pancreatic cancer cases were identified among Shanghai residency during 2004 to 2009. The crude incidence rate of pancreatic cancer was increasing from 12.80/100,000 in 2004 to 15.66/100,000 in 2009, while the standardized incidence rate was about 6.70/100,000 and didn't change a lot. The overall 5-year survival rate was 4.1% and the median survival time was 3.9 (95% Confidence Interval (CI) 3.8-4.0) months. Subjects had received surgical resection had improved survival (HR = 0.742, 95% CI: 0.634-0.868) than its counterparts. In adjusted multivariable Cox proportional-hazard models, factors

associated with poor survival included older age at diagnosis (age > = 70 years: hazard ratio (HR) = 1.827, 95% CI: 1.614-2.067), male sex (HR = 1.155, 95% CI: 1.041-1.281), distant disease at diagnosis (HR = 1.257, 95% CI: 1.061-1.488), positive lymph node (HR = 1.236, 95% CI: 1.085-1.408), tumor stage (Stage IV HR = 2.817, 95% CI: 2.029-3.909). CONCLUSION: The age-adjusted incidence rate was stable and overall survival rate was low among pancreatic cancer patients of Shanghai residency. Early detection and improved treatment strategies are needed to improve prognosis for this deadly disease.

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[294]

TÍTULO / TITLE: - FDG-PET/CT-based restaging may alter initial management decisions and clinical outcomes in patients with locally advanced pancreatic carcinoma planned to undergo chemoradiotherapy.

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

REVISTA / JOURNAL: - Cancer Imaging. 2013 Oct 4;13(3):423-8. doi: 10.1102/1470-7330.2013.0035.

●● Enlace al texto completo (gratuito o de pago) 1102/1470-7330.2013.0035

AUTORES / AUTHORS: - Topkan E; Parlak C; Yapar AF

INSTITUCIÓN / INSTITUTION: - Baskent University Adana Medical Faculty, Department of Radiation Oncology, Adana, Turkey.

RESUMEN / SUMMARY: - The impact of [(18)F]fluorodeoxyglucose-positron emission tomography (PET)/computed tomography (CT) restaging on management decisions and outcomes in patients with locally advanced pancreatic carcinoma (LAPC) scheduled for concurrent chemoradiotherapy (CRT) is examined. Seventy-one consecutive patients with conventionally staged LAPC were restaged with PET/CT before CRT, and were categorized into non-metastatic (M0) and metastatic (M1) groups. M0 patients received 50.4 Gy CRT with 5-fluorouracil followed by maintenance gemcitabine, whereas M1 patients received chemotherapy immediately or after palliative radiotherapy. In 19 patients (26.8%), PET/CT restaging showed distant metastases not detected by conventional staging. PET/CT restaging of M0 patients showed additional regional lymph nodes in 3 patients and tumors larger than CT-defined borders in 4. PET/CT therefore altered or revised initial management decisions in 26 (36.6%) patients. At median follow-up times of 11.3, 14.5, and 6.2 months for the entire cohort and the M0 and M1 cohorts, respectively, median overall survival was 16.1, 11.4, and 6.2 months, respectively; median locoregional progression-free survival was 9.9, 7.8, and 3.4 months, respectively; and median progression-free survival was 7.4, 5.1, and 2.5 months, respectively ($P < 0.05$ each). These findings suggest that PET/CT-based restaging may help select patients suitable for CRT, sparing those with metastases from futile radical protocols, and increasing the accuracy of estimated survival.

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[295]

TÍTULO / TITLE: - Stereotactic body radiotherapy in the treatment of Pancreatic Adenocarcinoma in elderly patients.

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

REVISTA / JOURNAL: - Radiat Oncol. 2013 Oct 16;8(1):240.

●● Enlace al texto completo (gratuito o de pago) 1186/1748-717X-8-240

AUTORES / AUTHORS: - Kim CH; Ling DC; Wegner RE; Flickinger JC; Heron DE; Zeh H; Moser AJ; Burton SA

RESUMEN / SUMMARY: - BACKGROUND: Treatment of pancreatic adenocarcinoma in the elderly is often complicated by comorbidities that preclude surgery, chemotherapy and/or conventional external beam radiation therapy (EBRT). Stereotactic body radiotherapy (SBRT) has thus garnered interest in this setting. METHODS: A retrospective review of 26 patients of age [greater than or equal to] 80 with pancreatic adenocarcinoma treated with definitive SBRT+/-chemotherapy from 2007--2011 was performed. Twenty-seven percent of patients were stage I, 38% were stage II, 27% were stage III and 8% were stage IV. Patients most commonly received 24Gy/1 fraction or 30-36Gy/3 fractions. Kaplan-Meier was used to estimate overall survival (OS), local control (LC), cause specific survival (CSS) and freedom-from-metastatic disease (FFMD). RESULTS: The median age was 86 (range 80--91), and median follow-up was 11.6 months (3.5-24.6). The median planning target volume was 21.48 cm3 (6.1-85.09). Median OS was 7.6 months with 6/12 month OS rates of 65.4%/34.6%, respectively. Median LC was 11.5 months, 6-month and 12-month actuarial LC rates were 60.1% and 41.2%, respectively. There were no independent predictors for LC, but there was a trend for improved LC with prescription dose greater than 20Gy (p = 0.063). Median CSS was 6.3 months, and 6-month and 12-month actuarial CSS were 53.8% and 23.1%, respectively. Median FFMD was 8.4 months, and 6-month and 12-month actuarial rates were 62.0 and 41.4%, respectively. Nine patients (47%) had local failures, 11 (58%) had distant metastasis, and 7 (37%) had both. There were no acute or late grade 3+ toxicities. CONCLUSIONS: Definitive SBRT is feasible, safe and effective in elderly patients who have unresectable disease, have comorbidities precluding surgery or decline surgery.

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[296]

TÍTULO / TITLE: - Capture, release and culture of circulating tumor cells from pancreatic cancer patients using an enhanced mixing chip.

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

REVISTA / JOURNAL: - Lab Chip. 2014 Jan 7;14(1):89-98. doi: 10.1039/c3lc51017d. Epub 2013 Nov 13.

●● Enlace al texto completo (gratuito o de pago) 1039/c3lc51017d

AUTORES / AUTHORS: - Sheng W; Ogunwobi OO; Chen T; Zhang J; George TJ; Liu C; Fan ZH

INSTITUCIÓN / INSTITUTION: - Interdisciplinary Microsystems Group, Department of Mechanical and Aerospace Engineering, University of Florida, P.O. Box 116250, Gainesville, FL 32611, USA. hfan@ufl.edu.

RESUMEN / SUMMARY: - Circulating tumor cells (CTCs) from peripheral blood hold important information for cancer diagnosis and disease monitoring. Analysis of this “liquid biopsy” holds the promise to usher in a new era of personalized therapeutic treatments and real-time monitoring for cancer patients. But the extreme rarity of CTCs in blood makes their isolation and characterization technologically challenging. This paper reports the development of a geometrically enhanced mixing (GEM) chip for high-efficiency and high-purity tumor cell capture. We also successfully demonstrated the release and culture of the captured tumor cells, as well as the isolation of CTCs from cancer patients. The high-performance microchip is based on geometrically optimized micromixer structures, which enhance the transverse flow and flow folding,

maximizing the interaction between CTCs and antibody-coated surfaces. With the optimized channel geometry and flow rate, the capture efficiency reached >90% with a purity of >84% when capturing spiked tumor cells in buffer. The system was further validated by isolating a wide range of spiked tumor cells (50-50 000) in 1 mL of lysed blood and whole blood. With the combination of trypsinization and high flow rate washing, captured tumor cells were efficiently released. The released cells were viable and able to proliferate, and showed no difference compared with intact cells that were not subjected to the capture and release process. Furthermore, we applied the device for detecting CTCs from metastatic pancreatic cancer patients' blood; and CTCs were found from 17 out of 18 samples (>94%). We also tested the potential utility of the device in monitoring the response to anti-cancer drug treatment in pancreatic cancer patients, and the CTC numbers correlated with the clinical computed tomograms (CT scans) of tumors. The presented technology shows great promise for accurate CTC enumeration, biological studies of CTCs and cancer metastasis, as well as for cancer diagnosis and treatment monitoring.

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[297]

TÍTULO / TITLE: - Identification of a novel subpopulation of tumor-initiating cells from gemcitabine-resistant pancreatic ductal adenocarcinoma patients.

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

REVISTA / JOURNAL: - PLoS One. 2013 Nov 21;8(11):e81283. doi: 10.1371/journal.pone.0081283.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0081283

AUTORES / AUTHORS: - Shimizu K; Chiba S; Hori Y

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Kobe Medical Center, Kobe, Japan ; Division of Medical Chemistry, Department of Biophysics, Kobe University Graduate School of Health Science, Kobe, Japan.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma is highly resistant to systemic chemotherapy. Although there are many reports using pancreatic cancer cells derived from patients who did not receive chemotherapy, characteristics of pancreatic cancer cells from chemotherapy-resistant patients remain unclear. In this study, we set out to establish a cancer cell line in disseminated cancer cells derived from gemcitabine-resistant pancreatic ductal adenocarcinoma patients. By use of in vitro co-culture system with stromal cells, we established a novel pancreatic tumor-initiating cell line. The cell line required its direct interaction with stromal cells for its in vitro clonogenic growth and passaging. Their direct interaction induced basal lamina-like extracellular matrix formation that maintained colony formation. The cell line expressed CD133 protein, which expression level changed autonomously and by culture conditions. These results demonstrated that there were novel pancreatic tumor-initiating cells that required direct interactions with stromal cells for their in vitro cultivation in gemcitabine-resistant pancreatic ductal adenocarcinoma. This cell line would help to develop novel therapies that enhance effects of gemcitabine or novel anti-cancer drugs.

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[298]

TÍTULO / TITLE: - A Study of Zoledronic Acid as Neo-Adjuvant, Perioperative Therapy in Patients with Resectable Pancreatic Ductal Adenocarcinoma.

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

REVISTA / JOURNAL: - J Cancer Ther. 2013 May;4(3):797-803.

●● Enlace al texto completo (gratuito o de pago) 4236/jct.2013.43096

AUTORES / AUTHORS: - Sanford DE; Porembka MR; Panni RZ; Mitchem JB; Belt BA; Plambeck-Suess SM; Lin G; Denardo DG; Fields RC; Hawkins WG; Strasberg SM; Lockhart AC; Wang-Gillam A; Goedegebuure SP; Linehan DC

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Washington University - School of Medicine.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic ductal adenocarcinoma (PDAC) is an aggressive malignancy characterized by abundant granulocytic myeloid-derived suppressor cells (G-MDSC = CD45+/Lin-/CD33+/CD11b+/CD15+), which infiltrate tumors and suppress anti-tumor immunity. We have previously demonstrated in a murine model of PDAC that zoledronic acid (ZA) depletes G-MDSC resulting in decreased tumor growth and improved survival. We report here the results of a phase 1 clinical trial (NCT00892242) using ZA as neo-adjuvant, perioperative therapy in patients with non-metastatic, resectable pancreatic adenocarcinoma. METHODS: Eligible PDAC patients received ZA (4mg) IV 2 weeks prior to surgery. Patients then received 2 additional doses of ZA 4 weeks apart. Blood and bone marrow were obtained from patients prior to treatment with ZA and 3 months after surgery for analysis of G-MDSC by flow cytometry. RESULTS: Twenty-three patients received pre-operative ZA with at least 6 months of follow-up Only 15 PDAC patients had non-metastatic PDAC, which was amenable to resection. ZA was well tolerated, and all adverse events were grade 1 or 2. The most common adverse events were fatigue, abdominal pain/discomfort, anorexia, and arthralgia. Of resected PDAC patients treated with ZA, 1- and 2-year overall survival (OS) was 85.7% and 33.3%, respectively, with a median OS of 18 months. This group had a 1- and 2-year progression-free survival (PFS) of 26.9% and 8.9%, respectively, with a median PFS of 12 months. The prevalence of G-MDSC was unchanged in the blood and bone marrow of PDAC patients pre- and post-treatment with ZA. CONCLUSION: ZA is safe and well tolerated as neo-adjuvant, peri-operative therapy in PDAC patients. In this small study, we did not observe a difference in OS or PFS compared to historical controls. Also, there was no difference in the prevalence of G-MDSC in the blood and bone marrow of PDAC patients pre- and post-treatment with ZA.

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[299]

TÍTULO / TITLE: - Pancreatic cancer: Adjuvant gemcitabine improves long-term outcomes of patients with resected pancreatic cancer.

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

REVISTA / JOURNAL: - Nat Rev Gastroenterol Hepatol. 2013 Nov 19. doi: 10.1038/nrgastro.2013.209.

●● Enlace al texto completo (gratuito o de pago) 1038/nrgastro.2013.209

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[300]

TÍTULO / TITLE: - External validation of the derived neutrophil to lymphocyte ratio as a prognostic marker on a large cohort of pancreatic cancer patients.

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

REVISTA / JOURNAL: - PLoS One. 2013 Nov 4;8(11):e78225. doi: 10.1371/journal.pone.0078225.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0078225

AUTORES / AUTHORS: - Szkandera J; Stotz M; Eisner F; Absenger G; Stojakovic T; Samonigg H; Kornprat P; Schaberl-Moser R; Alzoughbi W; Ress AL; Seggewies FS; Gerger A; Hoefler G; Pichler M

INSTITUCIÓN / INSTITUTION: - Division of Clinical Oncology, Department of Medicine, Medical University of Graz, Graz, Austria.

RESUMEN / SUMMARY: - BACKGROUND: With growing evidence on the role of inflammation in cancer biology, the presence of a systemic inflammatory response has been postulated as having prognostic significance in a wide range of cancer types. The derived neutrophil to lymphocyte ratio (dNLR), which represents an easily determinable potential prognostic marker in daily practise and clinical trials, has never been externally validated in pancreatic cancer (PC) patients. METHODS: Data from 474 consecutive PC patients, treated between 2004 and 2012 at a single centre, were evaluated retrospectively. Cancer-specific survival (CSS) was assessed using the Kaplan-Meier method. To evaluate the prognostic relevance of dNLR, univariate and multivariate Cox regression models were applied. RESULTS: We calculated by ROC analysis a cut-off value of 2.3 for the dNLR to be ideal to discriminate between patients' survival in the whole cohort. Kaplan-Meier curve reveals a dNLR>/=2.3 as a factor for decreased CSS in PC patients (p<0.001, log-rank test). An independent significant association between high dNLR>/=2.3 and poor clinical outcome in multivariate analysis (HR = 1.24, CI95% = 1.01-1.51, p = 0.041) was identified. CONCLUSION: In the present study we confirmed elevated pre-treatment dNLR as an independent prognostic factor for clinical outcome in PC patients. Our data encourage independent replication in other series and settings of this easily available parameter as well as stratified analysis according to tumor resectability.

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[301]

TÍTULO / TITLE: - A Novel Ras Inhibitor (MDC-1016) Reduces Human Pancreatic Tumor Growth in Mice.

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

REVISTA / JOURNAL: - Neoplasia. 2013 Oct;15(10):1184-95.

AUTORES / AUTHORS: - Mackenzie GG; Bartels LE; Xie G; Papayannis I; Alston N; Vrankova K; Ouyang N; Rigas B

INSTITUCIÓN / INSTITUTION: - Division of Cancer Prevention, Department of Medicine, Stony Brook University, Stony Brook, NY ; Department of Preventive Medicine, Stony Brook University, Stony Brook, NY.

RESUMEN / SUMMARY: - Pancreatic cancer has one of the poorest prognoses among all cancers partly because of its persistent resistance to chemotherapy. The currently limited treatment options for pancreatic cancer underscore the need for more efficient agents. Because activating Kras mutations initiate and maintain pancreatic cancer, inhibition of this pathway should have a major therapeutic impact. We synthesized phospho-farnesylthiosalicylic acid (PFTS; MDC-1016) and evaluated its efficacy, safety, and metabolism in preclinical models of pancreatic cancer. PFTS inhibited the growth of human pancreatic cancer cells in culture in a concentration- and time-dependent manner. In an MIA PaCa-2 xenograft mouse model, PFTS at a dose of 50 and 100 mg/kg significantly reduced tumor growth by 62% and 65% (P < .05 vs vehicle control). Furthermore, PFTS prevented pancreatitis-accelerated acinar-to-ductal metaplasia in mice with activated Kras. PFTS appeared to be safe, with the animals showing no signs of toxicity during treatment. Following oral administration,

PFTS was rapidly absorbed, metabolized to FTS and FTS glucuronide, and distributed through the blood to body organs. Mechanistically, PFTS inhibited Ras-GTP, the active form of Ras, both in vitro and in vivo, leading to the inhibition of downstream effector pathways c-RAF/mitogen-activated protein-extracellular signal-regulated kinase (ERK) kinase (MEK)/ERK1/2 kinase and phosphatidylinositol 3-kinase/AKT. In addition, PFTS proved to be a strong combination partner with phospho-valproic acid, a novel signal transducer and activator of transcription 3 (STAT3) inhibitor, displaying synergy in the inhibition of pancreatic cancer growth. In conclusion, PFTS, a direct Ras inhibitor, is an efficacious agent for the treatment of pancreatic cancer in preclinical models, deserving further evaluation.

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[302]

TÍTULO / TITLE: - Extracellular matrix specific protein fingerprints measured in serum can separate pancreatic cancer patients from healthy controls.

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

REVISTA / JOURNAL: - BMC Cancer. 2013 Nov 21;13(1):554. doi: 10.1186/1471-2407-13-554.

●● Enlace al texto completo (gratuito o de pago) 1186/1471-2407-13-554

AUTORES / AUTHORS: - Willumsen N; Bager CL; Leeming DJ; Smith V; Karsdal MA; Dornan D; Bay-Jensen AC

INSTITUCIÓN / INSTITUTION: - Nordic Bioscience A/S, Biomarkers & Research, Herlev Hovedgade 207, DK-2730 Herlev, Denmark. nwi@nordicbioscience.com.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer (PC) is an aggressive disease with an urgent need for biomarkers. Hallmarks of PC include increased collagen deposition (desmoplasia) and increased matrix metalloproteinase (MMP) activity. The aim of this study was to investigate whether protein fingerprints of specific MMP-generated collagen fragments differentiate PC patients from healthy controls when measured in serum. METHODS: The levels of biomarkers reflecting MMP-mediated degradation of type I (C1M), type III (C3M) and type IV (C4M, C4M12a1) collagen were assessed in serum samples from PC patients (n = 15) and healthy controls (n = 33) using well-characterized and validated competitive ELISAs. RESULTS: The MMP-generated collagen fragments were significantly elevated in serum from PC patients as compared to controls. The diagnostic power of C1M, C3M, C4M and C4M12 were >/=83% (p < 0.001) and when combining all biomarkers 99% (p < 0.0001). CONCLUSIONS: A panel of serum biomarkers reflecting altered MMP-mediated collagen turnover is able to differentiate PC patients from healthy controls. These markers may increase the understanding of mode of action of the disease and, if validated in larger clinical studies, provide an improved and additional tool in the PC setting.

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[303]

TÍTULO / TITLE: - Emerging therapies and latest development in the treatment of unresectable pancreatic neuroendocrine tumors: an update for clinicians.

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

REVISTA / JOURNAL: - Therap Adv Gastroenterol. 2013 Nov;6(6):474-90. doi: 10.1177/1756283X13498808.

●● Enlace al texto completo (gratuito o de pago) 1177 1756283X13498808 [pii

●● Enlace al texto completo (gratuito o de pago) 1177/1756283X13498808

AUTORES / AUTHORS: - Sharma J; Duque M; Saif MW

INSTITUCIÓN / INSTITUTION: - Tufts University School of Medicine, Tufts Medical Center, Boston, MA, USA.

RESUMEN / SUMMARY: - Pancreatic neuroendocrine tumors (pNETs) differ in their clinical behavior, presentation and prognosis based on their initial histological features and disease stage. While small resectable tumors can be treated surgically, metastatic and locally advanced disease carries a significant mortality and treatment options have been limited in terms of their efficacy. Streptozocin-based regimens were the only agents available before but recent advances have improved the armamentarium to treat pNETs. Newer chemotherapeutic agents such as temozolomide, somatostatin analogs and targeted therapies including everolimus and sunitinib are now available to treat these tumors. Several combination regimens with targeted therapies and newer agents such as pazopanib are being developed and tested in ongoing trials.

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[304]

TÍTULO / TITLE: - The Loss of miR-26a-Mediated Post-Transcriptional Regulation of Cyclin E2 in Pancreatic Cancer Cell Proliferation and Decreased Patient Survival.

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

REVISTA / JOURNAL: - PLoS One. 2013 Oct 8;8(10):e76450. doi: 10.1371/journal.pone.0076450.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0076450

AUTORES / AUTHORS: - Deng J; He M; Chen L; Chen C; Zheng J; Cai Z

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Changhai Hospital, Second Military Medical University, Shanghai, China.

RESUMEN / SUMMARY: - BACKGROUND: miR-26a plays a critical role in tumorigenesis, either as a tumor suppressor or as an oncogenic miRNA, depending on different tumor types. However, the function of miR-26a in pancreatic cancer has not been clearly elucidated. The present study was designed to determine the roles of miR-26a in pancreatic cancer and its association with the survival of patients with pancreatic cancer. METHODS: The expression of miR-26a was examined in 15 pairs of pancreatic duct adenocarcinoma (PDAC) and their adjacent benign pancreatic tissues (ABPT), by qRT-PCR. The results were confirmed by in situ hybridization using two panels of 106 PDACs and their ABPT microarray. The association of miR-26a expression with overall survival was determined. The proliferation and cell cycle distribution of Capan-2, SW-1990, and Panc-1 cells, transfected with miR-26a mimics or a miR-26a inhibitor, were assessed using the Cell Counting Kit-8 assay and flow cytometry, respectively. The cell tumorigenicity was evaluated via murine xenograft experiments. Cyclin D2, E2, EZH2, and PCNA levels were analyzed by Western blot and immunohistochemistry. RESULTS: miR-26a was expressed in the cytoplasm of pancreatic ductal epithelial cells, whereas its expression was significantly downregulated in PDAC tissues compared with that of ABPT. Patients with low miR-26a expression had a significantly shorter survival than those with high miR-26a expression. The in vitro and in vivo assays showed that overexpression of miR-26a resulted in cell cycle arrest, inhibited cell proliferation, and decreased tumor growth, which was associated with cyclin E2 downregulation. CONCLUSIONS: miR-26a is an important suppressor of pancreatic ductal carcinoma, and can prove to be a novel prognostic factor and therapeutic target for pancreatic cancer treatment.

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[305]

TÍTULO / TITLE: - Pancreatic cancer: Survival of patients with advanced pancreatic cancer is increased by nab-paclitaxel plus gemcitabine.

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

REVISTA / JOURNAL: - Nat Rev Gastroenterol Hepatol. 2013 Nov 19. doi: 10.1038/nrgastro.2013.223.

●● Enlace al texto completo (gratuito o de pago) 1038/nrgastro.2013.223

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[306]

TÍTULO / TITLE: - Pancreatic mucinous cystic tumor in Turner syndrome: How a tumor bends to a genetic disease.

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

REVISTA / JOURNAL: - Int J Surg Case Rep. 2013;4(11):1028-31. doi: 10.1016/j.ijscr.2013.09.003. Epub 2013 Sep 12.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ijscr.2013.09.003

AUTORES / AUTHORS: - Pizzi M; Pennelli G; Merante-Boschin I; Fassan M; Pelizzo MR; Rugge M

INSTITUCIÓN / INSTITUTION: - Department of Medicine DIMED, Surgical Pathology & Cytopathology Unit, University of Padova, Italy.

RESUMEN / SUMMARY: - INTRODUCTION: Mucinous cystic neoplasms (MCN) are uncommon tumors of the pancreatic corpus/tail occurring mostly in middle-aged women, with a variable clinico-biological behavior. On histology, MCNs concurrently show an epithelial mucosecreting component with ovarian-type stromal cells. PRESENTATION OF CASE: This report describes the first case of a pancreatic MCN with no ovarian-type stroma in a patient with Turner syndrome (TS). DISCUSSION: The mesenchymal component of MCN presumably results from the intra-pancreatic entrapment of ovarian stroma during embryogenesis. In our case, the absence of such stromal component may relate to the “dysgenetic” changes in the ovary involved in TS. CONCLUSION: The present case of primary pancreatic MCN arising in a TS-patient triggers some original speculation on the morphogenesis of pancreatic MCN, also expanding the current clinico-pathological knowledge of this extremely rare entity.

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[307]

TÍTULO / TITLE: - Digitoflavone Inhibits IkappaBalpha Kinase and Enhances Apoptosis Induced by TNFalpha through Downregulation of Expression of Nuclear Factor kappaB-Regulated Gene Products in Human Pancreatic Cancer Cells.

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

REVISTA / JOURNAL: - PLoS One. 2013 Oct 11;8(10):e77126. doi: 10.1371/journal.pone.0077126.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0077126

AUTORES / AUTHORS: - Cai X; Lu W; Yang Y; Yang J; Ye J; Gu Z; Hu C; Wang X; Cao P

INSTITUCIÓN / INSTITUTION: - Jiangsu Branch of China Academy of Chinese Medical Sciences, Nanjing, China ; Laboratory of Cellular and Molecular Biology, Jiangsu Province Academy of Traditional Chinese Medicine, Nanjing, China.

RESUMEN / SUMMARY: - Tumor necrosis factor-alpha (TNFalpha) activates both cell death and cell survival pathways. The activation of survival pathway renders most

cancer cells resistant to TNF-induced cytotoxicity. We found that pretreatment with digitoflavone, a plant flavonoid, greatly sensitized TNFalpha-induced apoptotic cell death in several human pancreatic cancer cells. In search of the molecular basis of the sensitization effect of digitoflavone, digitoflavone was found to inhibit TNFalpha-induced activation of nuclear transcription factor-kappa B (NF-kappaB) which is the main survival factor in TNFalpha signaling. NF-kappaB suppression occurred through inhibition of IkappaBalpha kinase activation, IkappaBalpha phosphorylation, IkappaBalpha degradation, and NF-kappaB nuclear translocation. This inhibition correlated with suppression of NF-kappaB-dependent genes involved in antiapoptosis (mcl-1, bcl-2, bcl-xl, c-iap1, c-iap2, flip, and survivin), proliferation (c-myc, cyclin d1), and angiogenesis (vegf, cox-2, and mmp-9). In addition, digitoflavone can activate JNK through inhibition of NF-kappaB signaling, provide a continuous blockade of the feed-back inhibitory mechanism by JNK-induced NF-kappaB activation. This study found a novel function of digitoflavone and enhanced the value of digitoflavone as an anticancer agent.

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[308]

TÍTULO / TITLE: - Successful Salvage Chemotherapy with FOLFIRINOX for Recurrent Mixed Acinar Cell Carcinoma and Ductal Adenocarcinoma of the Pancreas in an Adolescent Patient.

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

REVISTA / JOURNAL: - Case Rep Oncol. 2013 Sep 28;6(3):497-503. doi: 10.1159/000355320.

●● Enlace al texto completo (gratuito o de pago) 1159/000355320

AUTORES / AUTHORS: - Pfrommer S; Weber A; Dutkowski P; Schafer NG; Mullhaupt B; Bourquin JP; Breitenstein S; Pestalozzi BC; Stenner F; Renner C; D'Addario G; Graf HJ; Knuth A; Clavien PA; Samaras P

INSTITUCIÓN / INSTITUTION: - Department of Oncology, University Hospital Zurich, Switzerland.

RESUMEN / SUMMARY: - Pancreatic tumors are rare in children and adolescents. Here, we report the case of a 15-year-old boy who presented with a mixed acinar cell carcinoma/ductal adenocarcinoma with blastomatous components. He received multimodal treatment including various chemotherapy regimens and multistep surgery including liver transplantation. Introduction of FOLFIRINOX after relapse repeatedly achieved a durable metabolic and clinical response with good quality of life.

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[309]

TÍTULO / TITLE: - Solid pseudopapillary tumour of the pancreas: distinct patterns of computed tomography manifestation for male versus female patients.

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

REVISTA / JOURNAL: - Radiol Med. 2013 Nov 26.

●● Enlace al texto completo (gratuito o de pago) 1007/s11547-013-0327-2

AUTORES / AUTHORS: - Hu S; Huang W; Lin X; Wang Y; Chen KM; Chai W

INSTITUCIÓN / INSTITUTION: - Department of Radiology, The Affiliated Renmin Hospital, Jiangsu University, Zhenjiang, 212002, Jiangsu, China.

RESUMEN / SUMMARY: - PURPOSE: The purpose of this study was to retrospectively assess the features of computed tomography (CT) images and clinical characteristics of male patients with solid pseudopapillary tumours (SPTs) and compare them with

those of female patients. MATERIALS AND METHODS: Computed tomography images and clinical data of 102 patients with pathologically proven SPTs were reviewed. Details of the location, diameter, shape, encapsulation, calcification, internal composition, CT attenuation, and enhancement pattern of tumours were noted. Statistical analysis was performed using the chi 2 and t tests. RESULTS: Data from 16 males and 86 females were collected. Males were significantly older than females (38.5 years vs. 28.7 years; P = 0.004). Except for mean age, no significant statistical difference was observed between the clinical factors of SPTs in males and females. The mean tumour size in males was significantly smaller than that in females (5.3 vs. 7.6 cm; P = 0.037). Solid tumours were more common in males (8/16; 50 %) than in females (5/86; 5.8 %; P < 0.001). CONCLUSION: The imaging features of SPTs of males are different from those of females. In males, the finding of small, prominently solid tumours showing enhancement patterns typical of SPTs may suggest a diagnosis of SPT.

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[310]

TÍTULO / TITLE: - Antioxidant effect of mogrosides against oxidative stress induced by palmitic acid in mouse insulinoma NIT-1 cells.

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

REVISTA / JOURNAL: - Braz J Med Biol Res. 2013 Nov 18;0:0.

●● Enlace al texto completo (gratuito o de pago) 1590/1414-431X20133163

AUTORES / AUTHORS: - Xu Q; Chen SY; Deng LD; Feng LP; Huang LZ; Yu RR

INSTITUCIÓN / INSTITUTION: - Guilin Medical University, Department of Pharmacy, Guilin, China.

RESUMEN / SUMMARY: - Excessive oxidative stress in pancreatic beta cells, caused by glucose and fatty acids, is associated with the pathogenesis of type 2 diabetes. Mogrosides have shown antioxidant and antidiabetic activities in animal models of diabetes, but the underlying mechanisms remain unclear. This study evaluated the antioxidant effect of mogrosides on insulinoma cells under oxidative stress caused by palmitic acid, and investigated the underlying molecular mechanisms. Mouse insulinoma NIT-1 cells were cultured in medium containing 0.75 mM palmitic acid, mimicking oxidative stress. The effects of 1 mM mogrosides were determined with the dichlorodihydrofluorescein diacetate assay for intracellular reactive oxygen species (ROS) and FITC-Annexin V/PI assay for cell apoptosis. Expression of glucose transporter-2 (GLUT2) and pyruvate kinase was determined by semi-quantitative reverse-transcription polymerase chain reaction. Palmitic acid significantly increased intracellular ROS concentration 2-fold (P<0.05), and decreased expression of GLUT2 (by 60%, P<0.05) and pyruvate kinase (by 80%, P<0.05) mRNAs in NIT-1 cells. Compared with palmitic acid, co-treatment with 1 mM mogrosides for 48 h significantly reduced intracellular ROS concentration and restored mRNA expression levels of GLUT2 and pyruvate kinase. However, mogrosides did not reverse palmitic acid-induced apoptosis in NIT-1 cells. Our results indicate that mogrosides might exert their antioxidant effect by reducing intracellular ROS and regulating expression of genes involved in glucose metabolism. Further research is needed to achieve a better understanding of the signaling pathway involved in the antioxidant effect of mogrosides.

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[311]
TÍTULO / TITLE: - Secondary T-cell pancreatic lymphoma mimicking acute pancreatitis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - West Indian Med J. 2013 Jan;62(1):87-8.
AUTORES / AUTHORS: - Shao XN; Hu KY; Wu CJ; Shen Z; Chen WX
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, Zhejiang Province, China.

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[312]
TÍTULO / TITLE: - Recent Developments in Surgery: Minimally Invasive Approaches for Patients Requiring Pancreaticoduodenectomy.
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
- ●● Cita: JAMA: <> Surg. 2013 Oct 23. doi: 10.1001/jamasurg.2013.366.
- ●● Enlace al texto completo (gratuito o de pago) 1001/jamasurg.2013.366

AUTORES / AUTHORS: - Zenoni SA; Arnoletti JP; de la Fuente SG
INSTITUCIÓN / INSTITUTION: - Department of Surgical Oncology, Florida Hospital Orlando, Orlando.
RESUMEN / SUMMARY: - Over the past decade, minimally invasive surgery has been introduced as a means to allow manipulation of delicate tissues with outstanding visualization of the surgical field. The purpose of this article is to review the available literature regarding early postoperative outcomes and the technical challenges of minimally invasive pancreaticoduodenectomy, including robotic techniques. Herein, we provide a retrospective review of all published studies in the English literature in which a minimally invasive pancreaticoduodenectomy was performed. The reported advantages of minimally invasive pancreaticoduodenectomy include better visualization, faster recovery time, and decreased length of hospital stay. In cases of robotic approaches, some of the proposed advantages include increased dexterity and a superior ergonomic position for the operating surgeon. To our knowledge, few studies have reported results comparable to open techniques in oncologic outcomes with regard to the number of lymph nodes resected and clear margins obtained. An increasing number of pancreatic resections are being performed using minimally invasive approaches. It remains to be determined if the benefits of this technique outweigh its longer operative times and higher costs.

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[313]
TÍTULO / TITLE: - Endoscopic ultrasonography-guided cholecystogastrostomy in patients with unresectable pancreatic cancer using anti-migratory metal stents: A new approach.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Dig Endosc. 2013 Sep 18. doi: 10.1111/den.12163.
- ●● Enlace al texto completo (gratuito o de pago) 1111/den.12163

AUTORES / AUTHORS: - Widmer J; Alvarez P; Gaidhane M; Paddu N; Umrania H; Sharaiha R; Kahaleh M

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology and Hepatology, Weill Cornell Medical College, Cornell University, New York, USA.
RESUMEN / SUMMARY: - Cholecystectomy is contraindicated in patients with comorbidities or unresectable cancer. Percutaneous transhepatic gallbladder drainage (PTGBD) is typically offered with response rates ranging from 56% to 100%, but has several risks such as bleeding, pneumothorax, pneumoperitoneum, bile leak, and/or catheter migration. Endoscopic transpapillary gallbladder drainage (ETGD) and endoscopic ultrasound-guided transmural gallbladder drainage (EUS-GBD) are alternative endoscopic modalities that have a technical feasibility, efficacy and safety profile comparable with PTGBD. In this report, we present the first case series of transgastric EUS-GBD with placement of a fully covered self-expandable metal stent with anti-migratory fins. In three pancreatic cancercases with acute cholecystitis when ETGD was unsuccessful, there were no bile leaks or procedurally related complications. There were no acute cholecystitis recurrences. In conclusion, EUS-GBD is a promising, minimally invasive treatment for acute cholecystitis. Additional comparative studies are needed to validate the benefit of this technique.

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[314]
TÍTULO / TITLE: - CXCL12-CXCR4 Promotes Proliferation and Invasion of Pancreatic Cancer Cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5403-8.
AUTORES / AUTHORS: - Shen B; Zheng MQ; Lu JW; Jiang Q; Wang TH; Huang XE
INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, the Affiliated Jiangsu Cancer Hospital of Nanjing Medical University and Jiangsu Institute of Cancer Research, Nanjing, Jiangsu Province, China E-mail : huangxinen06@aliyun.com.
RESUMEN / SUMMARY: - Objective: CXCL12 exerts a wide variety of chemotactic effects on cells. Evidence indicates that CXCL12, in conjunction with its receptor, CXCR4, promotes invasion and metastasis of tumor cells. Our objective was to explore whether the CXCL12-CXCR4 biological axis might influence biological behavior of pancreatic cancer cells. Methods: Miapaca-2 human pancreatic cancer cells were cultured under three different conditions: normal medium (control), medium + recombinant CXCL12 (CXCL12 group), or medium + CXCR4-inhibitor AMD3100 (AMD3100 group). RT-PCR was applied to detect mRNA expression levels of CXCL12, CXCR4, matrix metalloproteinase 2 (MMP-2), MMP-9, and human urokinase plasminogen activator (uPA). Additionally, cell proliferation and invasion were performed using CCK-8 colorimetry and transwell invasion assays, respectively. Results: CXCL12 was not expressed in Miapaca-2 cells, but CXCR4 was detected, indicating that these cells are capable of receiving signals from CXCL12. Expression of extracellular matrix-degrading enzymes MMP-2, MMP- 9, and uPA was upregulated in cells exposed to exogenous CXCL12 ($P<0.05$). Additionally, both proliferation and invasion of pancreatic cancer cells were enhanced in the presence of exogenous CXCL12, but AMD3100 intervention effectively inhibited these processes ($P<0.05$). Conclusions: The CXCL12-CXCR4 biological axis plays an important role in promoting proliferation and invasion of pancreatic cancer cells.

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[315]

TÍTULO / TITLE: - Consistent Surgeon Evaluations of Three-Dimensional Rendering of PET/CT Scans of the Abdomen of a Patient with a Ductal Pancreatic Mass.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Sep 24;8(9):e75237. doi: 10.1371/journal.pone.0075237.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0075237
AUTORES / AUTHORS: - Wampole ME; Kairys JC; Mitchell EP; Ankeny ML; Thakur ML; Wickstrom E
INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Thomas Jefferson University, Philadelphia, Pennsylvania, United States of America.
RESUMEN / SUMMARY: - Two-dimensional (2D) positron emission tomography (PET) and computed tomography (CT) are used for diagnosis and evaluation of cancer patients, requiring surgeons to look through multiple planar images to comprehend the tumor and surrounding tissues. We hypothesized that experienced surgeons would consistently evaluate three-dimensional (3D) presentation of CT images overlaid with PET images when preparing for a procedure. We recruited six Jefferson surgeons to evaluate the accuracy, usefulness, and applicability of 3D renderings of the organs surrounding a malignant pancreas prior to surgery. PET/CT and contrast-enhanced CT abdominal scans of a patient with a ductal pancreatic mass were segmented into 3D surface renderings, followed by co-registration. Version A used only the PET/CT image, while version B used the contrast-enhanced CT scans co-registered with the PET images. The six surgeons answered 15 questions covering a) the ease of use and accuracy of models, b) how these models, with/without PET, changed their understanding of the tumor, and c) what are the best applications of the 3D visualization, on a scale of 1 to 5. The six evaluations revealed a statistically significant improvement from version A (score 3.6+/-0.5) to version B (score 4.4+/-0.4). A paired-samples t-test yielded $t(14) = -8.964$, $p<0.001$. Across the surgeon cohort, contrast-enhanced CT fused with PET provided a more lifelike presentation than standard CT, increasing the usefulness of the presentation. The experienced surgeons consistently reported positive reactions to 3D surface renderings of fused PET and contrast-enhanced CT scans of a pancreatic cancer and surrounding organs. Thus, the 3D presentation could be a useful preparative tool for surgeons prior to making the first incision. This result supports proceeding to a larger surgeon cohort, viewing prospective 3D images from multiple types of cancer.

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[316]
TÍTULO / TITLE: - Chin tremors associated with paroxetine in a patient with pancreatic adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):661-3. doi: 10.6092/1590-8577/1908.
AUTORES / AUTHORS: - John P; McConnell K; Saif MW
INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Tufts Medical Center. Boston, MA, USA. pjohn@tuftsmedicalcenter.org.
RESUMEN / SUMMARY: - CONTEXT: There have been many cases of medication-induced tremors. We report a patient who developed significant chin tremors after the administration of paroxetine. CASE REPORT: A 68-year-old Vietnamese female with a past medical history including GIST and pancreatic cancer status post Whipple procedure and six months of adjuvant chemotherapy with gemcitabine presented with

symptoms of anxiety for which she was treated with paroxetine. Within 2 weeks she developed chin tremors which resolved after paroxetine was discontinued. CONCLUSIONS: To our knowledge, this is the first case report of a temporary chin tremor associated with paroxetine. The exact mechanism of this phenomenon is unclear. However, it has been suggested that movement disorders such as chin tremors may be related to elevated serotonin levels causing an inhibition of central dopamine.

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[317]

TÍTULO / TITLE: - Commentary on “Microparticle-associated tissue factor activity in patients with metastatic pancreatic cancer and its effect on fibrin clot formation”

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

REVISTA / JOURNAL: - Transl Res. 2013 Oct 1. pii: S1931-5244(13)00335-6. doi: 10.1016/j.trsl.2013.09.011.

●● Enlace al texto completo (gratuito o de pago) 1016/j.trsl.2013.09.011

AUTORES / AUTHORS: - Soff GA

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

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[318]

TÍTULO / TITLE: - Ototoxicity associated with oxaliplatin in a patient with pancreatic cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):676-9. doi: 10.6092/1590-8577/1629.

AUTORES / AUTHORS: - Oh SY; Wasif N; Garcon MC; Rodriguez G; Saif MW

INSTITUCIÓN / INSTITUTION: - Department of Hematology/Oncology and Experimental Therapeutics, Tufts University School of Medicine. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - CONTEXT: Oxaliplatin, a third-generation platinum derivative is commonly used for the treatment of colorectal cancer, pancreatic cancer, upper gastrointestinal cancer, hepatobiliary cancer, and ovarian cancer. Neurotoxicity is the dose limiting toxicity and ototoxicity is very rare, less than 1% of patients. CASE REPORT: We present a case of a female patient with locally advanced unresectable pancreatic cancer who developed hearing loss after receiving oxaliplatin and gemcitabine. The dose of oxaliplatin was reduced but continued due to clinical benefit and radiological response. DISCUSSION: To the best of our knowledge, this is the third case report of oxaliplatin-induced ototoxicity. Ototoxicity seems to be a rare complication of oxaliplatin therapy. Regardless of its rare occurrence, clinicians should be aware of this severe complication and be diligent in monitoring patients’s clinical symptoms.

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[319]

TÍTULO / TITLE: - Synergism of cytotoxicity effects of triptolide and artesunate combination treatment in pancreatic cancer cell lines.

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

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5243-8.

AUTORES / AUTHORS: - Liu Y; Cui YF

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, The Second Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, China E-mail : Cuiyunfu1234@yahoo.cn.

RESUMEN / SUMMARY: - Background: Triptolide, extracted from the herb Tripteryglum wilfordii Hook.f that has long been used as a natural medicine in China, has attracted much interest for its anti-cancer effects against some kinds of tumours in recent years. Artesunate, extracted from the Chinese herb Artemisia annua, has proven to be effective and safe as an anti-malarial drug that possesses anticancer potential. The present study attempted to clarify if triptolide enhances artesunate-induced cytotoxicity in pancreatic cancer cell lines in vitro and in vivo. Methods: In vitro, to test synergic actions, cell viability and apoptosis were analyzed after treatment of pancreatic cancer cell lines with the two agents singly or in combination. The molecular mechanisms of apoptotic effects were also explored using qRT-PCR and Western blotting. In vivo, a tumor xenograft model was established in nude mice, for assessment of inhibitory effects of triptolide and artesunate. Results: We could show that the combination of triptolide and artesunate could inhibit pancreatic cancer cell line growth, and induce apoptosis, accompanied by expression of HSP 20 and HSP 27, indicating important roles in the synergic effects. Moreover, tumor growth was decreased with triptolide and artesunate synergy. Conclusion: Our result indicated that triptolide and artesunate in combination at low concentrations can exert synergistic anti-tumor effects in pancreatic cancer cells with potential clinical applications.

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[320]

TÍTULO / TITLE: - Reversing the Intractable Nature of Pancreatic Cancer by Selectively Targeting ALDH-High, Therapy-Resistant Cancer Cells.

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

REVISTA / JOURNAL: - PLoS One. 2013 Oct 23;8(10):e78130. doi: 10.1371/journal.pone.0078130.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0078130

AUTORES / AUTHORS: - Kim SK; Kim H; Lee DH; Kim TS; Kim T; Chung C; Koh GY; Kim H; Lim DS

INSTITUCIÓN / INSTITUTION: - Graduate School of Medical Science and Engineering, South Korea Advanced Institute of Science and Technology (KAIST), Daejeon, South Korea.

RESUMEN / SUMMARY: - Human pancreatic ductal adenocarcinoma (PDAC) is a cancer with a dismal prognosis. The efficacy of PDAC anticancer therapies is often short-lived; however, there is little information on how this disease entity so frequently gains resistance to treatment. We adopted the concept of cancer stem cells (CSCs) to explain the mechanism of resistance and evaluated the efficacy of a candidate anticancer drug to target these therapy-resistant CSCs. We identified a subpopulation of cells in PDAC with CSC features that were enriched for aldehyde dehydrogenase (ALDH), a marker expressed in certain stem/progenitor cells. These cells were also highly resistant to, and were further enriched by, treatment with gemcitabine. Similarly, surgical specimens from PDAC patients showed that those who had undergone preoperative chemo-radiation therapy more frequently displayed cancers with ALDH strongly positive subpopulations compared with untreated patients. Importantly, these ALDH-high cancer cells were sensitive to disulfiram, an ALDH inhibitor, when tested in

vitro. Furthermore, in vivo xenograft studies showed that the effect of disulfiram was additive to that of low-dose gemcitabine when applied in combination. In conclusion, human PDAC-derived cells that express high levels of ALDH show CSC features and have a key role in the development of resistance to anticancer therapies. Disulfiram can be used to suppress this therapy-resistant subpopulation.

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[321]

TÍTULO / TITLE: - The diversity between pancreatic head and body/tail cancers: clinical parameters and in vitro models.

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

REVISTA / JOURNAL: - Hepatobiliary Pancreat Dis Int. 2013 Oct;12(5):480-7.

AUTORES / AUTHORS: - Ling Q; Xu X; Zheng SS; Kalthoff H

INSTITUCIÓN / INSTITUTION: - Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, First Affiliated Hospital, Zhejiang University School of Medicine; Key Lab of Combined Multi-Organ Transplantation, Ministry of Public Health, Hangzhou, 310003, China. zyzss@zju.edu.cn.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic ductal adenocarcinoma (PDAC) can be divided into head, body and tail cancers according to the anatomy. Distinctions in tissue composition, vascularization and innervations have been clearly identified between the head and body/tail of the pancreas both in embryological development and in histopathology. To understand the postulated genotype difference, we present comprehensive information on two PDAC cell lines as typical representatives originating from pancreatic head and body/tail cancers, respectively. DATA SOURCE: In the present review, we compare the difference between pancreatic head and body/tail cancers regarding clinical parameters and introducing an in vitro model. RESULTS: Increasing evidence has shown that tumors at different locations (head vs body/tail) display different clinical presentation (e.g. incidence, symptom), treatment efficiency (e.g. surgery, chemotherapy) and thus patient prognosis. However, the genetic or molecular diversity (e.g. mutations, microRNA) between the two subtypes of PDAC has not been elucidated so far. They present different chemo- and/or radio-resistance, extracellular matrix adhesion and invasiveness, as well as genetic profiles. CONCLUSION: Genetic and tumor biological diversity exists in PDAC according to the tumor localization.

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[322]

TÍTULO / TITLE: - The relationship between lymphatic vascular density and vascular endothelial growth factor A (VEGF-A) expression with clinical-pathological features and survival in pancreatic adenocarcinomas.

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

REVISTA / JOURNAL: - Diagn Pathol. 2013 Oct 18;8(1):170.

●● Enlace al texto completo (gratuito o de pago) 1186/1746-1596-8-170

AUTORES / AUTHORS: - Zorgetto VA; Silveira GG; Oliveira-Costa JP; Soave DF; Soares FA; Ribeiro-Silva A

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is a rare tumor with an extremely low survival rate. Its known risk factors include the chronic use of tobacco and excessive alcohol consumption and the presence of chronic inflammatory diseases, such as pancreatitis and type 2 diabetes. Angiogenesis and

lymphangiogenesis, which have been the focus of recent research, are considered prognostic factors for cancer development. Knowing the angiogenic and lymphangiogenic profiles of a tumor may provide new insights for designing treatments according to the different properties of the tumor. The aim of this study was to evaluate the density of blood and lymphatic vessels, and the expression of VEGF-A, in pancreatic adenocarcinomas, as well as the relationship between blood and lymphatic vascular density and the prognostically important clinical-pathological features of pancreatic tumors. METHODS: Paraffin blocks containing tumor samples from 100 patients who were diagnosed with pancreatic cancer between 1990 and 2010 were used to construct a tissue microarray. VEGF expression was assessed in these samples by immunohistochemistry. To assess the lymphatic and vascular properties of the tumors, 63 cases that contained sufficient material were sectioned routinely. The sections were then stained with the D2-40 antibody to identify the lymphatic vessels and with a CD34 antibody to identify the blood vessels. The vessels were counted individually with the Leica Application Suite v4 program. All statistical analyses were performed using SPSS 18.0 (Chicago, IL, USA) software, and p values <= 0.05 were considered significant. RESULTS: In the Cox regression analysis, advanced age (p=0.03) and a history of type 2 diabetes (p=0.014) or chronic pancreatitis (p=0.02) were shown to be prognostic factors for pancreatic cancer. Blood vessel density (BVD) had no relationship with clinical-pathological features or death. Lymphatic vessel density (LVD) was inversely correlated with death (p=0.002), and by Kaplan-Meyer survival analysis, we found a significant association between low LVD (p=0.021), VEGF expression (p=0.023) and low patient survival. CONCLUSIONS: Pancreatic carcinogenesis is related to a history of chronic inflammatory processes, such as type 2 diabetes and chronic pancreatitis. In pancreatic cancer development, lymphangiogenesis can be considered an early event that enables the dissemination of metastases. VEGF expression and low LVD can be considered as poor prognostic factors as tumors with this profile are fast growing and highly aggressive.Virtual slides: The virtual slide(s) for this article can be found here: http://www.diagnosticpathology.diagnomx.eu/vs/5113892881028514.

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[323]

TÍTULO / TITLE: - 6]-Gingerol Prevents Disassembly of Cell Junctions and Activities of MMPs in Invasive Human Pancreas Cancer Cells through ERK/NF- kappa B/Snail Signal Transduction Pathway.

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

REVISTA / JOURNAL: - Evid Based Complement Alternat Med. 2013;2013:761852. doi: 10.1155/2013/761852. Epub 2013 Sep 24.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/761852

AUTORES / AUTHORS: - Kim SO; Kim MR

INSTITUCIÓN / INSTITUTION: - Department of Herbal Pharmacology, College of Oriental Medicine, Daegu Haany University, 165 Sang Dong, Suseong gu, Daegu 706-828, Republic of Korea.

RESUMEN / SUMMARY: - To study the effects of [6]-gingerol, a ginger phytochemical, on tight junction (TJ) molecules, we investigated TJ tightening and signal transduction pathways in human pancreatic duct cell-derived cancer cell line PANC-1. The following methods were utilized: MTT assay to determine cytotoxicity; zymography to examine matrix metalloproteinase (MMP) activities; transepithelial electrical resistance (TER)

and paracellular flux for TJ measurement; RT-PCR and immunoblotting for proteins related to TJ and invasion; and EMSA for NF- kappa B activity in PANC-1 cells. Results revealed that TER significantly increased and claudin 4 and MMP-9 decreased compared to those of the control. TJ protein levels, including zonula occludens (ZO-) 1, occludin, and E-cadherin, increased in [6]-gingerol-treated cells, which correlated with a decrease in paracellular flux and MMP activity. Furthermore, NF- kappa B/Snail nuclear translocation was suppressed via downregulation of the extracellular signal-regulated kinase (ERK) pathway in response to [6]-gingerol treatment. Moreover, treatment with U0126, an ERK inhibitor, completely blocked NF- kappa B activity. In conclusion, these findings demonstrate that [6]-gingerol regulates TJ-related proteins and suppresses invasion and metastasis through NF- kappa B/Snail inhibition via inhibition of the ERK pathway. Therefore, [6]-gingerol may suppress the invasive activity of PANC-1 cells.

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[324]

TÍTULO / TITLE: - The relationship between multiple clinicopathological features and nerve invasion in pancreatic cancer.

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

REVISTA / JOURNAL: - Hepatobiliary Pancreat Dis Int. 2013 Oct;12(5):546-51.

AUTORES / AUTHORS: - Wang PH; Song N; Shi LB; Zhang QH; Chen ZY

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Huashan Hospital, Fudan University, Shanghai 200040, China. shiliubin@medmail.com.cn.

RESUMEN / SUMMARY: - BACKGROUND: Nerve invasion is a specific type of tumor expansion and characteristic manifestation of pancreatic cancer (PC), with an incidence rate ranging from 50% to 100%. It is an important prognostic factor for pancreatic cancer, and its early detection is helpful in the management of the disease. This study was undertaken to analyze retrospectively the relationship between neural invasion and multiple clinicopathological features and to provide evidences for clinicians in the management of neural invasion in patients with PC. METHODS: Formalin-fixed paraffin-embeded specimens of PC taken from 215 patients were examined for the presence of neural invasion under a light microscope. Analyzed was the relationship between neural invasion and multiple clinicopathological feature including preoperative fasting blood glucose level, amylase level, serum CA19-9 level, abdominal pain, lumbar and back pain, and the expressions of p53 and Ki67 in tumor tissues. RESULTS: Preoperative fasting blood glucose level, serum CA19-9 level and p53 positive cells in cancer tissue were increased with the rise of pathological grade ($P<0.05$). These indices were significantly higher in patients with neural invasion than in those without ($P<0.05$). Further analysis revealed a positive correlation between p53 and Ki67 overexpression and lymphatic metastasis ($P<0.05$). Referred pain was positively correlated with neural invasion ($P<0.05$). Patients with PC perineural invasion were more likely to have a higher pathological grade ($P<0.05$). CONCLUSIONS: Our data indicated that the preoperative fasting blood glucose level, serum CA19-9 level, and referred pain are novel predictive markers for neural invasion in patients with PC. p53 and Ki67 play important roles in neural invasion of PC. Management of hyperglycemia may serve as an auxiliary treatment to curb neural invasion in PC.

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[325]

TÍTULO / TITLE: - Novel pancreatic cancer cell lines derived from genetically engineered mouse models of spontaneous pancreatic adenocarcinoma: applications in diagnosis and therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Nov 20;8(11):e80580. doi: 10.1371/journal.pone.0080580.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0080580
AUTORES / AUTHORS: - Torres MP; Rachagani S; Souchek JJ; Mallya K; Johansson SL; Batra SK
INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, Nebraska, United States of America.
RESUMEN / SUMMARY: - Pancreatic cancer (PC) remains one of the most lethal human malignancies with poor prognosis. Despite all advances in preclinical research, there have not been significant translation of novel therapies into the clinics. The development of genetically engineered mouse (GEM) models that produce spontaneous pancreatic adenocarcinoma (PDAC) have increased our understanding of the pathogenesis of the disease. Although these PDAC mouse models are ideal for studying potential therapies and specific genetic mutations, there is a need for developing syngeneic cell lines from these models. In this study, we describe the successful establishment and characterization of three cell lines derived from two (PDAC) mouse models. The cell line UN-KC-6141 was derived from a pancreatic tumor of a Kras(G12D);Pdx1-Cre (KC) mouse at 50 weeks of age, whereas UN-KPC-960 and UN-KPC-961 cell lines were derived from pancreatic tumors of Kras(G12D);Trp53(R172H);Pdx1-Cre (KPC) mice at 17 weeks of age. The cancer mutations of these parent mice carried over to the daughter cell lines (i.e. Kras(G12D) mutation was observed in all three cell lines while Trp53 mutation was observed only in KPC cell lines). The cell lines showed typical cobblestone epithelial morphology in culture, and unlike the previously established mouse PDAC cell line Panc02, expressed the ductal marker CK19. Furthermore, these cell lines expressed the epithelial-mesenchymal markers E-cadherin and N-cadherin, and also, Muc1 and Muc4 mucins. In addition, these cell lines were resistant to the chemotherapeutic drug Gemcitabine. Their implantation in vivo produced subcutaneous as well as tumors in the pancreas (orthotopic). The genetic mutations in these cell lines mimic the genetic compendium of human PDAC, which make them valuable models with a high potential of translational relevance for examining diagnostic markers and therapeutic drugs.

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[326]
TÍTULO / TITLE: - Suppression of metastasis of human pancreatic cancer cells to the liver by small interfering RNA-mediated targeting of the midkine gene.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Oncol Lett. 2013 Nov;6(5):1338-1342. Epub 2013 Sep 12.
●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1572
AUTORES / AUTHORS: - Yu L; Fan Y; Chen B; Hu Y; Gao Y; Wei D
INSTITUCIÓN / INSTITUTION: - Zhenjiang Key Laboratory of Molecular Endocrinology, Zhenjiang, Jiangsu 212001, P.R. China.
RESUMEN / SUMMARY: - The present study aimed to ascertain whether suppression of midkine (MK) expression in pancreatic cancer cells inhibits metastasis to the liver. Human pancreatic cancer AsPC-1 cells were transfected with small interfering RNA

(siRNA) targeting MK. siRNA against MK was observed to reduce the expression of MK mRNA and protein in a concentration- and time-dependent manner, and to decrease the number of migrating and tissue-penetrating cells in a concentration-dependent manner (P<0.005). Extracellular vascular endothelial growth factor (VEGF) concentrations were markedly reduced for the siRNA-transfected cells compared with those that were non-siRNA-transfected. The liver transmission rate and tumor nodule number in the animals harboring the siRNA-transfected cells were lower compared with those in the animals harboring the non-siRNA-transfected cells (P<0.005). These data indicate that metastasis of pancreatic cancer cells to the liver requires the expression of MK. The downregulation of VEGF expression is essential to the mechanism whereby suppression of MK expression constrains the metastasis of pancreatic cancer cells to the liver.

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[327]

TÍTULO / TITLE: - Histone deacetylase 6 and cytoplasmic linker protein 170 function together to regulate the motility of pancreatic cancer cells.

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

REVISTA / JOURNAL: - Protein Cell. 2013 Nov 21.

●● Enlace al texto completo (gratuito o de pago) 1007/s13238-013-3098-6

AUTORES / AUTHORS: - Li D; Sun X; Zhang L; Yan B; Xie S; Liu R; Liu M; Zhou J

INSTITUCIÓN / INSTITUTION: - Department of Genetics and Cell Biology, College of Life Sciences, Nankai University, Tianjin, 300071, China.

RESUMEN / SUMMARY: - Pancreatic cancer is a devastating disease with the worst prognosis among all the major human malignancies. The propensity to rapidly metastasize contributes significantly to the highly aggressive feature of pancreatic cancer. The molecular mechanisms underlying this remain elusive, and proteins involved in the control of pancreatic cancer cell motility are not fully characterized. In this study, we find that histone deacetylase 6 (HDAC6), a member of the class II HDAC family, is highly expressed at both protein and mRNA levels in human pancreatic cancer tissues. HDAC6 does not obviously affect pancreatic cancer cell proliferation or cell cycle progression. Instead, it significantly promotes the motility of pancreatic cancer cells. Further studies reveal that HDAC6 interacts with cytoplasmic linker protein 170 (CLIP-170) and that these two proteins function together to stimulate the migration of pancreatic cancer cells. These findings provide mechanistic insight into the progression of pancreatic cancer and suggest HDAC6 as a potential target for the management of this malignancy.

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[328]

TÍTULO / TITLE: - Knockdown of RON receptor kinase delays but does not prevent tumor progression while enhancing HGF/MET signaling in pancreatic cancer cell lines.

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

REVISTA / JOURNAL: - Oncogenesis. 2013 Oct 7;2:e76. doi: 10.1038/oncsis.2013.36.

●● Enlace al texto completo (gratuito o de pago) 1038/oncsis.2013.36

AUTORES / AUTHORS: - Zhao S; Cao L; Freeman JW

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Division of Medical Oncology, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA.

RESUMEN / SUMMARY: - In this study, the role of RON (receptor originated from nantes) in tumor progression was further investigated in context with MET expression

and activity. RON and MET expressions were not detected in an immortalized normal human pancreas cell line (HPNE), but were co-expressed in five of seven pancreatic ductal adenocarcinoma (PDAC) cell lines (PANC-1, BxPC-3, Capan-2, CFPAC-1 and AsPC-1). RON expression was knocked down by an shRNA approach in two PDAC cell lines (BxPC-3 and CFPAC-1) that co-express MET. Knockdown of RON significantly inhibited cell growth, clonogenicity and macrophage stimulating protein (MSP), RON ligand induced invasion by in vitro assays and significantly inhibited tumor growth ($P<0.001$) and metastasis ($P<0.009$) in an orthotopic pancreatic cancer mouse model at week 7. However, by week 9, the mice implanted with RON knockdown cells had developed similar size primary tumors and metastases compared with that seen in the control group at week 7. Western blotting and immunohistochemistry analyses showed that MET remains highly expressed in cells and tumor tissues where RON was knocked down. Moreover, knockdown of RON did not prevent hepatocyte growth factor (HGF) stimulated invasion in in vitro Matrigel assays. Treating cells with MSP induced the transphosphorylation of MET, suggesting that signaling may be modulated by relative levels of RON and MET receptors and their corresponding ligands. To this point, HGF treatment of RON knockdown cells caused an increase in intensity and duration of MET signaling, suggesting that MET signaling may compensate for loss of RON signaling. Treatment of cells with an MET inhibitor, PHA-665752, had minimal effects on inhibiting cell growth but significantly inhibited cell invasion induce by ligands for either MET or RON. These results suggest that HGF/MET signaling may have a more important role in tumor cell invasion and metastasis rather than in tumor cell proliferation. This study indicates that specific inhibition of RON delays but does not prevent progression of PDAC. Moreover, specific signaling may be modulated by the interaction of RON and MET receptors. This dynamic interaction of RON and MET in pancreatic cancer cells suggests that dual targeting of both RON and MET will be preferable to inhibition of either target alone.

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[329]

TÍTULO / TITLE: - Clinical, molecular and genetic validation of a murine orthotopic xenograft model of pancreatic adenocarcinoma using fresh human specimens.

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

REVISTA / JOURNAL: - PLoS One. 2013 Oct 18;8(10):e77065. doi: 10.1371/journal.pone.0077065.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0077065

AUTORES / AUTHORS: - Walters DM; Stokes JB; Adair SJ; Stelow EB; Borgman CA; Lowrey BT; Xin W; Blais EM; Lee JK; Papin JA; Parsons JT; Bauer TW

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Virginia, Charlottesville, Virginia, United States of America.

RESUMEN / SUMMARY: - BACKGROUND: Relevant preclinical models that recapitulate the key features of human pancreatic ductal adenocarcinoma (PDAC) are needed in order to provide biologically tractable models to probe disease progression and therapeutic responses and ultimately improve patient outcomes for this disease. Here, we describe the establishment and clinical, pathological, molecular and genetic validation of a murine, orthotopic xenograft model of PDAC. METHODS: Human PDACs were resected and orthotopically implanted and propagated in immunocompromised mice. Patient survival was correlated with xenograft growth and metastatic rate in mice. Human and mouse tumor pathology were compared. Tumors

were analyzed for genetic mutations, gene expression, receptor tyrosine kinase activation, and cytokine expression. RESULTS: Fifteen human PDACs were propagated orthotopically in mice. Xenograft-bearing mice developed peritoneal and liver metastases. Time to tumor growth and metastatic efficiency in mice each correlated with patient survival. Tumor architecture, nuclear grade and stromal content were similar in patient and xenografted tumors. Propagated tumors closely exhibited the genetic and molecular features known to characterize pancreatic cancer (e.g. high rate of KRAS, P53, SMAD4 mutation and EGFR activation). The correlation coefficient of gene expression between patient tumors and xenografts propagated through multiple generations was 93 to 99%. Analysis of gene expression demonstrated distinct differences between xenografts from fresh patient tumors versus commercially available PDAC cell lines. CONCLUSIONS: The orthotopic xenograft model derived from fresh human PDACs closely recapitulates the clinical, pathologic, genetic and molecular aspects of human disease. This model has resulted in the identification of rational therapeutic strategies to be tested in clinical trials and will permit additional therapeutic approaches and identification of biomarkers of response to therapy.

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[330]

TÍTULO / TITLE: - MicroRNA-375 targets the 3-phosphoinositide-dependent protein kinase-1 gene in pancreatic carcinoma.

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

REVISTA / JOURNAL: - Oncol Lett. 2013 Oct;6(4):953-959. Epub 2013 Aug 2.

●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1510

AUTORES / AUTHORS: - Song SD; Zhou J; Zhou J; Zhao H; Cen JN; Li DC

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, The First Affiliated Hospital of Soochow University, Jiangsu 215006, P.R. China.

RESUMEN / SUMMARY: - Pancreatic carcinoma (PC) is an aggressive malignancy with one of the poorest mortality rates. It is the sixth leading cause of mortality from malignant disease in China and the fourth leading cause of cancer-related mortality in the United States. The poor outcome reflects the requirement for an improved understanding of the transcriptional control of oncogenic signaling pathways. 3-phosphoinositide-dependent protein kinase-1 (PDK1) is a potent oncogenic driver of PC. The present study aimed to elucidate the transcriptional regulation of microRNA (miR)-375-targeted PDK1. miR-375 is a putative target and, in the present study, was observed to be significantly downregulated in the tumor compared with non-tumor tissues from patients with PC (n=44). As determined by a luciferase reporter assay, the ectopic expression of miR-375 was identified to diminish the transcriptional activity of PDK1. Furthermore, immunoblotting revealed that miR-375 suppressed endogenous PDK1 protein levels. Functional assays showed that miR-375 was able to inhibit proliferation and promote apoptosis of the PC cells. miR-375 is a significant regulator of the PDK1 oncogene, suggesting that it may have a potential therapeutic role in the treatment of PC.

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[331]

TÍTULO / TITLE: - Preoperative CEA and CA 19-9 are prognostic markers for survival after curative resection for ductal adenocarcinoma of the pancreas - A retrospective tumor marker prognostic study.

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

REVISTA / JOURNAL: - Int J Surg. 2013 Oct 23. pii: S1743-9191(13)01078-9. doi: 10.1016/j.ijsu.2013.10.005.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ijsu.2013.10.005

AUTORES / AUTHORS: - Distler M; Pilarsky E; Kersting S; Grutzmann R

INSTITUCIÓN / INSTITUTION: - Department of General, Thoracic and Vascular Surgery, University Hospital Carl Gustav Carus, TU Dresden, Germany. Electronic address: marius.distler@uniklinikum-dresden.de.

RESUMEN / SUMMARY: - BACKGROUND: The prognosis for patients with ductal adenocarcinoma of the pancreas (PDAC) remains poor even after curative resection. Carbohydrate antigen 19-9 (CA 19-9) and the carcinoembryonic antigen (CEA) are the most widely used serum-based tumor markers for the diagnosis and follow up of pancreatic cancer. In our analysis we aim to assess the prognostic value of a combination of both tumor markers in patients with pancreatic ductal adenocarcinoma (PDAC). PATIENTS AND METHODS: Between 01/1995 and 08/2012 we performed a total of 264 pancreatic resections due to PDAC. Patients were stratified into 3 groups in regard to their preoperative tumor marker levels. Survival was compared between the groups using Kaplan Meier analysis and log rank test. Univariate subgroup analysis and multivariate analysis were performed. RESULTS: For 259 cases complete follow up could be obtained. In patients with low preoperative CEA and CA 19-9 levels (group 1 n = 91) the mean survival was 33.3 month (CI 95% 25.1-41.5). If one of the analyzed tumor markers (CEA/CA19-9) was preoperatively elevated above the cut-off level (group 2 n = 106) mean survival was 28.5 month (CI 95% 22.1-35.1). 62 patients showed preoperative elevation of both, CEA and CA 19-9 (group 3); mean survival in this group was 23.9 month (CI 95% 13.9-33.9), p > 0.01. Multivariate analysis confirmed preoperative CEA/CA 19-9 level as independent prognostic factor (HR 1.299). CONCLUSION: Preoperative CEA and CA 19-9 levels correlate with patient prognosis after curative pancreatic resection due to PDAC. This is especially true for the most frequently pT ¾ stages of PDAC. Even if CEA and CA 19-9 might not be appropriate for screening, its serum levels should therefore be determined prior to operation and taken into account when resectability or operability is doubtful.

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[332]

TÍTULO / TITLE: - Down-regulation of miR-221 inhibits proliferation of pancreatic cancer cells through up-regulation of PTEN, p27(kip1), p57(kip2), and PUMA.

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

REVISTA / JOURNAL: - Am J Cancer Res. 2013 Nov 1;3(5):465-77.

AUTORES / AUTHORS: - Sarkar S; Dubaybo H; Ali S; Goncalves P; Kollepara SL; Sethi S; Philip PA; Li Y

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Barbara Ann Karmanos Cancer Institute, Wayne State University School of Medicine Detroit, MI, USA.

RESUMEN / SUMMARY: - Pancreatic cancer is the fourth leading cause of cancer related death in the US and exhibits aggressive features with short survival rate and high mortality. Therefore, it is important to understand the molecular mechanism(s) involved in the aggressive growth of pancreatic cancers, and further design novel targeted therapies for its treatment with better treatment outcome. In the present study, we found that the expression of miR-221 was significantly up-regulated in pancreatic cancer cell lines and tumor tissues compared to normal pancreatic duct epithelial cells and normal pancreas tissues. Moreover, we found that the pancreatic cancer patients

with high miR-221 expression had a relatively shorter survival compared to those with lower expression, suggesting that miR-221 could be an oncogenic miRNA and a prognostic factor for poor survival of patients. Interestingly, transfection of miR-221 inhibitor suppressed the proliferative capacity of pancreatic cancer cells with concomitant up-regulation of PTEN, p27(kip1), p57(kip2), and PUMA, which are the tumor suppressors and the predicted targets of miR-221. Most importantly, we found that the treatment of pancreatic cancer cells with isoflavone mixture (G2535), formulated 3,3'-diindolylmethane (BR-DIM), or synthetic curcumin analogue (CDF) could down-regulate the expression of miR-221 and consequently up-regulate the expression of PTEN, p27(kip1), p57(kip2), and PUMA, leading to the inhibition of cell proliferation and migration of MiaPaCa-2 and Panc-1 cells. These results provide experimental evidence in support of the oncogenic role of miR-221 and also demonstrate the role of isoflavone, BR-DIM, and CDF as potential non-toxic agents that are capable of down-regulation of miR-221. Therefore, these agents combined with conventional chemotherapeutics could be useful in designing novel targeted therapeutic strategy for the treatment of pancreatic cancer for which there is no curative therapy.

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[333]

TÍTULO / TITLE: - Neoadjuvant radiation therapy and its impact on complications after pancreaticoduodenectomy for pancreatic cancer: analysis of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP).

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

REVISTA / JOURNAL: - HPB (Oxford). 2013 Sep 24. doi: 10.1111/hpb.12141.

●● Enlace al texto completo (gratuito o de pago) 1111/hpb.12141

AUTORES / AUTHORS: - Cho SW; Tzeng CW; Johnston WC; Cassera MA; Newell PH; Hammill CW; Wolf RF; Aloia TA; Hansen PD

INSTITUCIÓN / INSTITUTION: - Hepatobiliary and Pancreatic Surgery Program, Providence Cancer Center, Portland, OR, USA.

RESUMEN / SUMMARY: - OBJECTIVES: This study investigated the impact of neoadjuvant radiation therapy (XRT) on postoperative outcomes following pancreaticoduodenectomy for pancreatic cancer. METHODS: The American College of Surgeons National Quality Improvement Program database was queried for the period 2005-2010 to assess complication rates following pancreaticoduodenectomy for pancreatic cancer. Two groups of patients were identified, comprising those who received neoadjuvant XRT and those who did not (control group). RESULTS: A total of 4416 patients were identified, including 200 in the XRT group and 4216 in the control group. There were differences in patient characteristics between the groups, including in age, hypertension and bilirubin level. Despite the fact that weight loss was more common, median operative time was longer (423 min versus 368 min; P < 0.001), and vascular reconstruction was more commonly required (20.5% versus 8.4%; P < 0.001) in the XRT group. In addition, the XRT group had a shorter median hospital stay than the control group (9 days versus 10 days; P = 0.005). Mortality (3.0% versus 2.7%; P = 0.818) and morbidity (40.5% versus 37.6%; P = 0.404) rates were not influenced by neoadjuvant XRT. Blood transfusion rates were increased in the XRT group (13.0% versus 7.4%; P = 0.003). Severe complications were influenced by age >70 years, American Society of Anesthesiologists (ASA) class >2, preoperative sepsis, dyspnoea, weight loss, impaired functional status, peripheral vascular disease and operative time

of >8 h. CONCLUSIONS: Neoadjuvant XRT is not associated with an increase in complications after pancreaticoduodenectomy.

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[334]

TÍTULO / TITLE: - HBV- and HCV-Related Infections and Risk of Pancreatic Cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):603-9. doi: 10.6092/1590-8577/1948.

AUTORES / AUTHORS: - Fiorino S; Cuppini A; Castellani G; Bacchi-Reggiani ML; Jovine E

INSTITUCIÓN / INSTITUTION: - Unit of Internal Medicine, Hospital of Budrio. Budrio, BO, Italy. sirio.fiorino@ausl.bologna.it.

RESUMEN / SUMMARY: - Pancreatic carcinoma is one of the most lethal cancers in humans. The poor prognosis of this malignancy depends on several factors, such as: lack of early symptoms, advanced stage at detection, early metastatic spread and no effective systemic treatment. To date, only few risk factors for this malignancy are known; therefore, considerable efforts are required to identify additional causative agents involved in the process of pancreatic carcinogenesis. In the last years, a large series of epidemiological investigations have suggested that both bacteria and viruses may play a important role in the initiation and progression of several animal and human cancers. In particular, some studies have showed that hepatitis B (HBV) and hepatitis C (HCV) viruses, two hepatotropic pathogens with well-known oncogenic properties for liver, may be detected also in extra-hepatic tissues, such as pancreas. The aim of this paper is to briefly report the results of available studies, assessing the possible association between HBV/HCV and pancreatic cancer development as well as to discuss the limiting factors of these researches.

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[335]

TÍTULO / TITLE: - Solid-pseudopapillary neoplasm of the pancreas - comparisons between magnetic resonance and histological findings.

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

REVISTA / JOURNAL: - Pol J Pathol. 2013 Nov;64(3):216-23.

AUTORES / AUTHORS: - Burdan F; Mocarska A; Guz E; Paluszkiewicz P; Terlecki P; Patyra K; Janczarek M; Zelazowska-Cieslinska I; Szubstarski F; Szumilo J; Staroslawska E

INSTITUCIÓN / INSTITUTION: - Prof. Justyna Szumilo MD, PhD, Department of Clinical Pathomorphology, Medical University of Lublin, Jaczewskiego 8, 20-059 Lublin, Poland, tel. +48 81 718 73 25, fax +48 81 718 73 24, e-mail: jszumilo@wp.pl.

RESUMEN / SUMMARY: - Solid-pseudopapillary neoplasm is a rare pancreatic tumor typically observed in young adults. A new case of the tumor was diagnosed in a 22-year-old woman. An abnormal mass connected with the pancreatic body was found on ultrasound and computed tomography. Magnetic resonance revealed weak homogeneous contrast enhancement and a low ADC value (0.824 mm/s2; b1000). Primary radiological diagnosis suggested a solid pancreatic neoplasm, which was confirmed during histopathological assessment after resection of the pancreatic body with preservation of the spleen and normal drainage through the main pancreatic duct. Histological appearance of the solid-pseudopapillary neoplasm corresponded with its radiological morphology.

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[336]

TÍTULO / TITLE: - uPAR-controlled oncolytic adenoviruses eliminate cancer stem cells in human pancreatic tumors.

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

REVISTA / JOURNAL: - Stem Cell Res. 2013 Sep 27;12(1):1-10. doi: 10.1016/j.scr.2013.09.008.

●● Enlace al texto completo (gratuito o de pago) 1016/j.scr.2013.09.008

AUTORES / AUTHORS: - Sobrevals L; Mato-Berciano A; Urtasun N; Mazo A; Fillat C

INSTITUCIÓN / INSTITUTION: - Institut d'Investigacions Biomediques August Pi i Sunyer-IDIBAPS, Barcelona, España; Centro de Investigacion Biomedica en Red de Enfermedades Raras (CIBERER), Barcelona, España.

RESUMEN / SUMMARY: - Pancreatic tumors contain cancer stem cells highly resistant to chemotherapy. The identification of therapies that can eliminate this population of cells might provide with more effective treatments. In the current work we evaluated the potential of oncolytic adenoviruses to act against pancreatic cancer stem cells (PCSC). PCSC from two patient-derived xenograft models were isolated from orthotopic pancreatic tumors treated with saline, or with the chemotherapeutic agent gemcitabine. An enrichment in the number of PCSC expressing the cell surface marker CD133 and a marked enhancement on tumorsphere formation was observed in gemcitabine treated tumors. No significant increase in the CD44, CD24, and epithelial-specific antigen (ESA) positive cells was observed. Neoplastic sphere-forming cells were susceptible to adenoviral infection and exposure to oncolytic adenoviruses resulted in elevated cytotoxicity with both Adwt and the tumor specific AduPARE1A adenovirus. In vivo, intravenous administration of a single dose of AduPARE1A in human-derived pancreatic xenografts led to a remarkable anti-tumor effect. In contrast to gemcitabine AduPARE1A treatment did not result in PCSC enrichment. No enrichment on tumorspheres neither on the CD133+ population was detected. Therefore our data provide evidences of the relevance of uPAR-controlled oncolytic adenoviruses for the elimination of pancreatic cancer stem cells.

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[337]

TÍTULO / TITLE: - An Interesting Clinical Entity of Squamous Cell Cancer of the Pancreas with Liver and Bone Metastases: a Case Report and Review of the Literature.

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

REVISTA / JOURNAL: - J Gastrointest Cancer. 2013 Nov 16.

●● Enlace al texto completo (gratuito o de pago) 1007/s12029-013-9560-0

AUTORES / AUTHORS: - Thomas D; Shah N; Shaaban H; Maroules M

INSTITUCIÓN / INSTITUTION: - Department of Medicine, St. Joseph's Regional Medical Center, 703 Main St, Paterson, NJ, 07503, USA, David.Thomas@techdolphin.com.

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[338]

TÍTULO / TITLE: - Pain affecting procedures in non-resectable pancreatic carcinoma.

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

REVISTA / JOURNAL: - Khirurgiia (Sofiia). 2013;(2):26-30.

AUTORES / AUTHORS: - Plachkov I; Chernopolski P; Bozhkov V; Madjov R

INSTITUCIÓN / INSTITUTION: - Second Department of Surgery, UMHAT Saint Marina, Varna, Bulgaria. iplachkov@mail.bg

RESUMEN / SUMMARY: - Pancreatic cancer is third most common cancer of the gastrointestinal tract in Bulgaria, accouting for 11, 6% in 2008. The leading symptom in patients with pancreatic cancer is the pain. The pain can be related with neoplasms and their metastasis. We should use all kind of resourses for pain relief: conventional drugs (according to the three steps strategy of WHO), interventional or surgical procedures. AIM: To present the interventional and surgical techniques in our practice and to share our experience for pain control in patients with nonresectable pancreatic cancer to improve their quality of life. MATERIAL: In a seven year period (2004-2011) we performed 59 thoracoscopic splanhnicectomies/30--bilateral/ 4 intraoperative resections of celiac ganglion, 25 CT—control celiac plexus neurolysis and 90 cases pain relief with epidural analgesia. Concerning the quality of life we applied a questionnaire of a spannish medical center " City of Hope" adapted for patients with cancer and the level of pain with visual analogue scale VAS. RESULTS: The long-term duration of the pain relief technique depends on applied technic, of cancer invasion and of the technic itself. The technique with the longest effect are the intraoperative celiac ganglion removal and the bilateral thoracoscopic splanhnicectomy. On the other hand the shortest effect we report the celiac plexus neurolysis, and the epudural analgesia. These data are in correlation with the reduction of the pain shown using VAS thus improving the quality of life. CONCLUSIONS: The surgical and interventional methods for control of cancer pain have their own collocation improving the quality of life of these patients. New strategies for the pain control are need in the future.

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[339]

TÍTULO / TITLE: - Is superior mesenteric artery reimplantation during surgery for pancreaticoduodenal tumors an underutilized procedure?

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

REVISTA / JOURNAL: - Indian J Gastroenterol. 2013 Nov 12.

●● Enlace al texto completo (gratuito o de pago) 1007/s12664-013-0431-1

AUTORES / AUTHORS: - Govil S

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, Bangalore Institute of Oncology, 8 Kalinga Rao Road, Sampangiramnagar, Bangalore, 560 027, India, s4govil@gmail.com.

RESUMEN / SUMMARY: - Resection and reimplantation of the superior mesenteric artery (SMA) as part of a pancreaticoduodenal resection for cancer is rarely performed even in high-volume centers because of the risks inherent in this procedure and the perceived lack of oncological benefit associated with arterial resection during pancreaticoduodenectomy. The role of arterial resection during pancreaticoduodenectomy has recently been reevaluated, and this procedure may be of greater benefit than previously believed in selected patients. It also has a definite role when necessary to resect low-grade pancreatic and peripancreatic malignancies or to salvage intraoperative injury to the SMA. This small case series presents the authors experience with this procedure.

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[340]

TÍTULO / TITLE: - Escin Chemosensitizes Human Pancreatic Cancer Cells and Inhibits the Nuclear Factor-kappaB Signaling Pathway.

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

REVISTA / JOURNAL: - Biochem Res Int. 2013;2013:251752. Epub 2013 Oct 27.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/251752

AUTORES / AUTHORS: - Rimmon A; Vexler A; Berkovich L; Earon G; Ron I; Lev-Ari S

INSTITUCIÓN / INSTITUTION: - Laboratory of Herbal Medicine and Cancer Research, Institute of Oncology, Tel Aviv Sourasky Medical Center, 6 Weizmann Street, 64239 Tel Aviv, Israel ; Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

RESUMEN / SUMMARY: - Background. There is an urgent need to develop new treatment strategies and drugs for pancreatic cancer that is highly resistant to radio-chemotherapy. Aesculus hippocastanum (the horse chestnut) known in Chinese medicine as a plant with anti-inflammatory, antiedema, antianalgesic, and antipyretic activities. The main active compound of this plant is Escin (C54H84O23). Objective. To evaluate the effect of Escin alone and combined with chemotherapy on pancreatic cancer cell survival and to unravel mechanism(s) of Escin anticancer activity. Methods. Cell survival was measured by XTT colorimetric assay. Synergistic effect of combined therapy was determined by CalcuSyn software. Cell cycle and induction of apoptosis were evaluated by FACS analysis. Expression of NF- kappa B-related proteins (p65, I kappa Balpha, and p-I kappa Balpha) and cyclin D was evaluated by western blot analysis. Results. Escin decreased the survival of pancreatic cancer cells with IC50 = 10-20 M. Escin combined with gemcitabine showed only additive effect, while its combination with cisplatin resulted in a significant synergistic cytotoxic effect in Panc-1 cells. High concentrations of Escin induced apoptosis and decreased NF- kappa B-related proteins and cyclin D expression. Conclusions. Escin decreased pancreatic cancer cell survival, induced apoptosis, and downregulated NF- kappa B signaling pathway. Moreover, Escin sensitized pancreatic cancer cells to chemotherapy. Further translational research is required.

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[341]

TÍTULO / TITLE: - Diagnostic and therapeutic implications of a novel immunohistochemical panel detecting duodenal mucosal invasion by pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Int J Clin Exp Pathol. 2013 Oct 15;6(11):2476-86.

AUTORES / AUTHORS: - Sopha SC; Gopal P; Merchant NB; Revetta FL; Gold DV; Washington K; Shi C

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Microbiology and Immunology, Vanderbilt University Medical Center Nashville, TN, USA.

RESUMEN / SUMMARY: - BACKGROUND: We investigated a series of pancreaticoduodenectomy and duodenal biopsies with a panel of immunohistochemical markers to identify duodenal mucosal invasion by pancreatic ductal adenocarcinoma (PDAC), including markers of poor prognosis and targets of promising novel immunotherapies. MATERIALS AND METHODS: Eighteen consecutive pancreaticoduodenectomy specimens with duodenal mucosal invasion by PDAC were examined for expression of MUC1, MUC4, MUC5AC, MUC6, mesothelin, MUC2, CDX2, and DPC4 on formalin-fixed, paraffin-embedded sections of duodenal-ampullary-pancreatic junctions. Expression of all but MUC6 was also assessed in

duodenal biopsies from 12 patients with duodenal mucosal invasion by PDAC. RESULTS: The duodenal mucosa expressed MUC1 (crypts), MUC2 (goblet cells), MUC6 (Brunner glands), CDX2, and DPC4. PDACs in the duodenal mucosa from the resection (n=16-18) and biopsy (n=12) specimens were marked as follows: MUC1 100% (30/30), MUC4 83% (24/29), MUC5AC 83% (25/30), mesothelin 82% (23/28), MUC2 7% (2/30), and CDX2 36% (10/28). Loss of DPC4 expression was seen in 16 of 29 (55%) cases. Reactive mucosa adjacent to PDAC expressed MUC4, MUC5AC and mesothelin in 65% (17/26), 19% (5/27), and 19% (5/26) of cases, respectively. While MUC5AC and mesothelin had high diagnostic accuracy for detection of PDAC, MUC2, CDX2 and DPC4 expression demonstrated negative correlation with PDAC, with absent expression being highly specific for PDAC. CONCLUSION: Immunohistochemical labeling for PDAC biomarkers may aid the diagnosis of PDAC in duodenal biopsy, especially in situations where diagnosis of a pancreatic mass is challenging.

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[342]
TÍTULO / TITLE: - Pancreatic cancer in Saudi Arabia.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Saudi Med J. 2013 Nov;34(11):1199-200.
AUTORES / AUTHORS: - Meshikhes AN; Alfaifi SA; Alghamdi HJ; Jazieh AM
INSTITUCIÓN / INSTITUTION: - Department of Surgery, King Fahad Specialist Hospital, Dammam, Kingdom of Saudi Arabia.

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[343]
TÍTULO / TITLE: - Metformin targets the metabolic achilles heel of human pancreatic cancer stem cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Oct 18;8(10):e76518. doi: 10.1371/journal.pone.0076518.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0076518
AUTORES / AUTHORS: - Lonardo E; Cioffi M; Sancho P; Sanchez-Ripoll Y; Trabulo SM; Dorado J; Balic A; Hidalgo M; Heeschen C
INSTITUCIÓN / INSTITUTION: - Stem Cells & Cancer Group, Molecular Pathology Programme, Spanish National Cancer Research Centre (CNIO), Madrid, España.
RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinomas contain a subset of exclusively tumorigenic cancer stem cells (CSCs), which are capable of repopulating the entire heterogeneous cancer cell populations and are highly resistant to standard chemotherapy. Here we demonstrate that metformin selectively ablated pancreatic CSCs as evidenced by diminished expression of pluripotency-associated genes and CSC-associated surface markers. Subsequently, the ability of metformin-treated CSCs to clonally expand in vitro was irreversibly abrogated by inducing apoptosis. In contrast, non-CSCs preferentially responded by cell cycle arrest, but were not eliminated by metformin treatment. Mechanistically, metformin increased reactive oxygen species production in CSC and reduced their mitochondrial transmembrane potential. The subsequent induction of lethal energy crisis in CSCs was independent of AMPK/mTOR. Finally, in primary cancer tissue xenograft models metformin effectively reduced tumor burden and prevented disease progression; if combined with a stroma-

targeting smoothened inhibitor for enhanced tissue penetration, while gemcitabine actually appeared dispensable.

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[344]

TÍTULO / TITLE: - “Total arterial devascularization first” technique for resection of pancreatic head cancer during pancreaticoduodenectomy.

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

REVISTA / JOURNAL: - J Huazhong Univ Sci Technolog Med Sci. 2013 Oct;33(5):687-91. doi: 10.1007/s11596-013-1181-0. Epub 2013 Oct 20.

●● Enlace al texto completo (gratuito o de pago) 1007/s11596-013-1181-0

AUTORES / AUTHORS: - Peng F; Wang M; Zhu F; Tian R; Shi CJ; Xu M; Wang X; Shen M; Hu J; Peng SY; Qin RY

INSTITUCIÓN / INSTITUTION: - Department of Pancreatic-Biliary Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030, China, Nicholas.peng7@hotmail.com.

RESUMEN / SUMMARY: - Integrated resection of the pancreatic head is the most difficult step in radical pancreaticoduodenectomy (RPD) in patients with the portal vein (PV) and superior mesenteric vein (SMV) invasion or oppression by the tumor. This study introduced a new idea and skill named the “total arterial devascularization first” (TADF) technique and its applications in RPD. Three arterial blood supplies of pancreatic head were obstructed before dissection of veins. The critical steps included exposure of the anterior surface of the abdominal aorta (AA) by completely transecting neural and connective tissue between superior mesenteric artery (SMA) and pancreatic mesounsinate, and transection of the mesounsinate from the origin of SMA to the root of the celiac trunk. From January 2012 through May 2013, a total of 58 patients with PV/SMV invasion or oppression underwent RPD using this technique. The median operative time was 5.1 h (ranging 4.5-8.1 h). The median intraoperative blood loss was 450 mL (ranging 200-900 mL). No intraoperative and postoperative bleeding of pancreatic head region occurred. Among the 58 patients, 21 were subjected to vessel lateral wall angiectomy or angiorrhaphy, and 10 to angiectomy and end-to-end anastomosis. The incidence of postoperative bleeding, postoperative pancreatic fistula and biliary fistula was 5.2%, 6.8%, and 1.7%, respectively. No patients died 3 months after operation. The TADF technique is a new method for intricate RPD and could improve the security of surgery and reduce intraoperative bleeding, which is expected to become standardized surgical approach for RPD.

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[345]

TÍTULO / TITLE: - Synergistic combination of valproic acid and oncolytic parvovirus H-1PV as a potential therapy against cervical and pancreatic carcinomas.

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

REVISTA / JOURNAL: - EMBO Mol Med. 2013 Oct;5(10):1537-55. doi: 10.1002/emmm.201302796. Epub 2013 Sep 17.

●● Enlace al texto completo (gratuito o de pago) 1002/emmm.201302796

AUTORES / AUTHORS: - Li J; Bonifati S; Hristov G; Marttila T; Valmary-Degano S; Stanzel S; Schnolzer M; Mougin C; Aprahamian M; Grekova SP; Raykov Z; Rommelaere J; Marchini A

INSTITUCIÓN / INSTITUTION: - Infection and Cancer Program, Tumor Virology Division (F010), German Cancer Research Center (DKFZ), Heidelberg, Germany.
RESUMEN / SUMMARY: - The rat parvovirus H-1PV has oncolytic and tumour-suppressive properties potentially exploitable in cancer therapy. This possibility is being explored and results are encouraging, but it is necessary to improve the oncotoxicity of the virus. Here we show that this can be achieved by co-treating cancer cells with H-1PV and histone deacetylase inhibitors (HDACIs) such as valproic acid (VPA). We demonstrate that these agents act synergistically to kill a range of human cervical carcinoma and pancreatic carcinoma cell lines by inducing oxidative stress, DNA damage and apoptosis. Strikingly, in rat and mouse xenograft models, H-1PV/VPA co-treatment strongly inhibits tumour growth promoting complete tumour remission in all co-treated animals. At the molecular level, we found acetylation of the parvovirus nonstructural protein NS1 at residues K85 and K257 to modulate NS1-mediated transcription and cytotoxicity, both of which are enhanced by VPA treatment. These results warrant clinical evaluation of H-1PV/VPA co-treatment against cervical and pancreatic ductal carcinomas.

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[346]
TÍTULO / TITLE: - Overexpression of COL11A1 by Cancer-Associated Fibroblasts: Clinical Relevance of a Stromal Marker in Pancreatic Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Oct 23;8(10):e78327. doi: 10.1371/journal.pone.0078327.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0078327
AUTORES / AUTHORS: - Garcia-Pravia C; Galvan JA; Gutierrez-Corral N; Solar-Garcia L; Garcia-Perez E; Garcia-Ocana M; Del Amo-Iribarren J; Menendez-Rodriguez P; Garcia-Garcia J; de Los Toyos JR; Simon-Buela L; Barneo L
INSTITUCIÓN / INSTITUTION: - Pathological Anatomy Service, Hospital Universitario Central de Asturias (HUCA), Oviedo, España ; Instituto Universitario de Oncologia del Principado de Asturias (IUOPA), Oviedo, España.
RESUMEN / SUMMARY: - BACKGROUND: The collagen11A1 (COL11A1) gene is overexpressed in pancreatic cancer. The expression of COL11A1 protein could be involved in desmoplastic events in pancreatic cancer, but an antibody that specifically stains the COL11A1 protein is not currently available. METHODS AND FINDINGS: A total of 54 pancreatic ductal adenocarcinomas (PDAC), 23 chronic pancreatitis (CP) samples, and cultured peritumoral stromal cells of PDAC (passages 3-6) were studied. Normal human pancreas tissue samples were obtained through a cadaveric organ donation program. 1) Validation of COL11A1 gene overexpression by q-RT-PCR. FINDINGS: the expression of COL11A1 gene is significantly increased in PDAC samples vs. normal and CP samples. 2) Analysis of COL11A1 by immunohistochemistry using highly specific anti-proCOL11A1 antibodies. FINDINGS: anti-proCOL11A1 stains stromal cells/cancer-associated fibroblasts (CAFs) of PDAC but it does not stain chronic benign condition (chronic pancreatitis) stromal cells, epithelial cells, or normal fibroblasts. 3) Evaluation of the discrimination ability of the antibody. FINDINGS: anti-proCOL11A1 immunostaining accurately discriminates between PDAC and CP (AUC 0.936, 95% CI 0.851, 0.981). 4) Phenotypic characterization of proCOL11A1+ stromal cells co-staining with mesenchymal, epithelial and stellate cell markers on pancreatic tissue samples and cultured

peritumoral pancreatic cancer stromal cells. FINDINGS: ProCOL11A1+ cells present co-staining with mesenchymal, stellate and epithelial markers (EMT phenotype) in different proportions. CONCLUSIONS/SIGNIFICANCE: Detection of proCOL11A1 through immunostaining with this newly-developed antibody allows for a highly accurate distinction between PDAC and CP. Unlike other available antibodies commonly used to detect CAFs, anti-proCOL11A1 is negative in stromal cells of the normal pancreas and almost absent in benign inflammation. These results strongly suggest that proCOL11A1 is a specific marker for CAFs, and thus, anti-proCOL11A1 is a powerful new tool for cancer research and clinical diagnostics.

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[347]

TÍTULO / TITLE: - Overexpression of IQGAP1 in human pancreatic cancer.

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

REVISTA / JOURNAL: - Hepatobiliary Pancreat Dis Int. 2013 Oct;12(5):540-5.

AUTORES / AUTHORS: - Wang XX; Li XZ; Zhai LQ; Liu ZR; Chen XJ; Pei Y

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Shanxi Medical University, Taiyuan 030001, China. wxiaoxia99007@yahoo.com.cn.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is a highly aggressive malignant tumor with the lowest survival rate. A better understanding of the molecular mechanisms which contribute to pancreatic cancer occurrence and progression will aid in the development of new approaches to the early diagnosis, prevention, and treatment of this deadly disease. The scaffold protein IQGAP1 shows elevated levels in a variety of cancer types. Currently, we investigated whether or not IQGAP1 is also overexpressed in pancreatic cancer. METHODS: IQGAP1 expression was examined in pancreatic cancer and normal tissues adjacent to cancerous tissues (adjacent tissues) by Western blotting and real-time RT-PCR as well as in paraffin sections of tissue microarray by immunohistochemistry. The correlations between IQGAP1 expression and various clinicopathological characteristics were analyzed. RESULTS: Western blotting and real-time RT-PCR revealed that the levels of IQGAP1 protein and mRNA expression in pancreatic cancer tissues were significantly increased compared with adjacent tissues. Immunohistochemistry analysis on tissue microarray showed that IQGAP1 protein expression was significantly higher in pancreatic cancer (80.0%, 48/60) compared with adjacent tissues (18.3%, 11/60) ($P<0.001$). Moreover, overexpression of IQGAP1 was shown to be associated with the grades of tumor differentiation ($P<0.05$). CONCLUSION: The overexpression of IQGAP1 may play an important role in pancreatic cancer occurrence and progression, and IQGAP1 may serve as a novel molecular target for the diagnosis and treatment of pancreatic cancer.

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[348]

TÍTULO / TITLE: - Significance of caveolin-1 regulators in pancreatic cancer.

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

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4501-7.

AUTORES / AUTHORS: - Chen T; Liu L; Xu HX; Wang WQ; Wu CT; Yao WT; Yu XJ

INSTITUCIÓN / INSTITUTION: - Department of Pancreas and Hepatobiliary Surgery, Fudan University Shanghai Cancer Center, Shanghai, China E-mail : yuxianjun88@hotmail.com.

RESUMEN / SUMMARY: - Caveolin-1 is a scaffold protein on the cell membrane. As the main component of caveolae, caveolin-1 is involved in many biological processes that include substance uptake and transmembrane signaling. Many of these processes and thus caveolin-1 contribute to cell transformation, tumorigenesis, and metastasis. Of particular interest are the dual rolesof tumor suppressor and oncogene that caveolin-1 appear to play in different malignancies, including pancreatic cancer. Therefore, analyzing caveolin-1 regulators and understanding their mechanisms of actionis key to identifying novel diagnostic and therapeutic tools for pancreatic cancer. This review details the mechanisms of action of caveolin-1 regulators and the potential significance for pancreatic cancer treatment.

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[349]
TÍTULO / TITLE: - A duodenal mass and acute pancreatitis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Turk J Gastroenterol. 2013 Jun;24(3):299-301.
AUTORES / AUTHORS: - Cakir OO; Biyik M; Gungor G; Ataseven H; Demir A; Tavli L
INSTITUCIÓN / INSTITUTION: - Selcuk University, Meram School of Medicine, Department of Gastroenterology and Hepatology, Konya, Turkey.
RESUMEN / SUMMARY: - To the Editor, Eosinophilic gastroenteritis (EGE) is a rare condition, first described in 1937 by Kaijser et al.It is defined as a disorder primarily affecting the gastrointestinal tract with eosinophil-rich inflammation, in the absence of known causes of eosinophilia (e.g. drug reactions, parasitic infections, or malignancy) (1). Three different forms of EGE can be distinguished: mucosal disease, muscle layer disease, and subserosal disease. The symptoms of EGE are related to the layer involved. Mucosal disease is the most common form and presents with nonspecific symptoms such as abdominal pain, nausea, vomiting, diarrhea, or malabsorption. The second form, muscle layer disease, is a more serious form that presents with symptoms due to intestinal obstruction. The third form, subserosal disease, is uncommon and presents with ascites. The incidence of EGE in the USA is approximately 2,5 per 100.000 adults (2,3). A 56-year-old man was admitted with a history of abdominal pain, nausea, and vomiting for 3 months. He had experienced postprandial fullness for the past month and lost 6 kg in weight. He had no prior history of drug use. He had no history of food allergies. His clinical examination was remarkable for abdominal distension and mild upper abdominal tenderness with palpation. Laboratory tests on admission revealed a WBC count of 21780/mm3 with an eosinophil count of 0.8% (normal 0.5%-6%). Serum amylase was 757 U/L (normal 28-100 U/L) and serum lipase was 386 U/L (normal 22-51 U/L). Serum IgE level was 650 U/L (normal < 140 U/L). Other laboratory tests including liver function tests, routine stool studies, serum lipid profile, and serum immunoglobulins, were normal. An ultrasound and CT scan of the abdomen revealed a dilated stomach with retained food and mild thickening of the duodenal folds. The pancreas was normal, and there were no gallstones. The patient was treated conservatively with rehydration and nasogastric suction. EGD showed ulcers and thickened duodenal folds with duodenal narrowing. Multiple 2-6 mm ulcerated nodules were noted in the duodenum, with thickening of the duodenal folds extending into the second part of the duodenum (Figure 1 A, B). Biopsies of the duodenum showed chronic duodenitis with intense eosinophilic infiltration of the lamina propria and muscularis mucosa (Figure 2 A, B). The patient

was treated with steroids, and his symptoms of duodenal obstruction resolved. In EGE, eosinophilia is present in 80% of cases. Further investigations should include endoscopy for mucosal biopsy. To confirm the diagnosis of EGE, other causes leading to eosinophilic infiltration of the bowel must be ruled out, such as food allergy, drug idiosyncrasies, parasitic / helminthic infestation, connective tissue disorders, vasculitis malignancy, Crohn's disease, and non-tropical sprue. Another important differential diagnosis is the hypereosinophilic syndrome. The syndrome presents with longer than 6 months of persistent eosinophilia and may also be present in extraintestinal organs (skin, lymph nodes, heart, lungs, liver, spleen, central nervous system, etc.) (4,5). We underline the importance of recognising EGE, since proper treatment can prevent further mucosal damage and progression to severe malabsorption and malnutrition. In our case, eosinophilic infiltration in the duodenum, resulting in luminal obstruction of the second part of duodenum, was encountered as a complication of acute pancreatitis. This is a rare condition. In conclusion, the diagnosis of eosinophilic gastroenteritis should be considered in the patients with a duodenal mass.

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[350]

TÍTULO / TITLE: - mTOR plays critical roles in pancreatic cancer stem cells through specific and stemness-related functions.

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

REVISTA / JOURNAL: - Sci Rep. 2013 Nov 15;3:3230. doi: 10.1038/srep03230.

●● Enlace al texto completo (gratuito o de pago) 1038/srep03230

AUTORES / AUTHORS: - Matsubara S; Ding Q; Miyazaki Y; Kuwahata T; Tsukasa K; Takao S

INSTITUCIÓN / INSTITUTION: - Cancer and Regenerative Medicine, Frontier Biomedical Science and Swine Research Center, Sakuragaoka, Kagoshima, 890-8520, Japan.

RESUMEN / SUMMARY: - Pancreatic cancer is characterized by near-universal mutations in KRAS. The mammalian target of rapamycin (mTOR), which functions downstream of RAS, has divergent effects on stem cells. In the present study, we investigated the significance of the mTOR pathway in maintaining the properties of pancreatic cancer stem cells. The mTOR inhibitor, rapamycin, reduced the viability of CD133(+) pancreatic cancer cells and sphere formation which is an index of self-renewal of stem-like cells, indicating that the mTOR pathway functions to maintain cancer stem-like cells. Further, rapamycin had different effects on CD133(+) cells compared to cyclopamine which is an inhibitor of the Hedgehog pathway. Thus, the mTOR pathway has a distinct role although both pathways maintain pancreatic cancer stem cells. Therefore, mTOR might be a promising target to eliminate pancreatic cancer stem cells.

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[351]

TÍTULO / TITLE: - shRNA-mediated silencing inhibits migration, but not invasiveness of human pancreatic cancer cells.

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

REVISTA / JOURNAL: - Chin J Cancer Res. 2013 Oct;25(5):514-519.

●● Enlace al texto completo (gratuito o de pago) 3978/j.issn.1000-9604.2013.09.03

AUTORES / AUTHORS: - Xie J; Chen Z; Liu L; Li P; Zhu X; Gao H; Meng Z

INSTITUCIÓN / INSTITUTION: - Department of Integrative Oncology, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, China;

RESUMEN / SUMMARY: - OBJECTIVE: Early metastasis is a major biological feature of pancreatic cancer. The current study examined whether silencing Slc38a1, a gene involved in energy metabolism, using short hairpin RNA (shRNA) could inhibit the growth, migration, and invasiveness of pancreatic cancer cells. METHODS: A series of Slc38a1 shRNAs were designed and cloned into the pGPU6/GFP/Neo vectors. An shRNA with the most efficacious inhibitory action on SCL38A1 expression (65% inhibition) upon screening in DH5alpha bacteria was used to transfect SW1990 human pancreatic cancer cells. Cell growth, migration, and invasiveness were examined using cell counting kit-8, Boyden chamber without and with Matrigel, respectively. RESULTS: Transfection of SW1990 cells with the SLCs38A1 shRNA significantly decreased the proliferation (P<0.0001) and migratory potential (by 46.7%, P=0.0399) of the cancer cells. Invasiveness, however, was not affected. CONCLUSIONS: Inhibiting Slc38a1 using shRNA technology could decrease the growth and migration of representative pancreatic cancer cells. However, the fact that invasiveness was not affected suggested that SLC38A1 is unlikely to be responsible for early metastasis.

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[352]

TÍTULO / TITLE: - Upregulation of Wnt5a promotes epithelial-to-mesenchymal transition and metastasis of pancreatic cancer cells.

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

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 25;13(1):496.

●● Enlace al texto completo (gratuito o de pago) 1186/1471-2407-13-496

AUTORES / AUTHORS: - Bo H; Zhang S; Gao L; Chen Y; Zhang J; Chang X; Zhu M

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is one of the most lethal cancers worldwide. The aim of this study was to determine the expression pattern, clinical significance, and biological functions of Wnt5a in pancreatic cancer. METHODS: Immunohistochemistry was performed to examine Wnt5a expression in 134 surgically resected pancreatic adenocarcinoma and adjacent normal pancreatic tissues. Associations of Wnt5a expression with clinicopathological factors and cancer-specific survival were analyzed. The effects of Wnt5a overexpression or silencing on the invasiveness and epithelial-to-mesenchymal transition (EMT) of pancreatic cancer cells were studied. Silencing of beta-catenin by small interfering RNA was done to determine its role in the Wnt5a-mediated tumor phenotype. RESULTS: The percentage of Wnt5a positive expression showed a bell-shaped pattern in pancreatic cancer tissues, peaking in well-differentiated carcinomas. The median cancer-specific survival was comparable between patients with positive versus negative expression of Wnt5a. Overexpression of Wnt5a promoted the migration and invasion of pancreatic cancer cells, whereas Wnt5a depletion had an inhibitory effect. In an orthotopic pancreatic cancer mouse model, Wnt5a overexpression resulted in increased invasiveness and metastasis, coupled with induction of EMT in tumor cells. Treatment with recombinant Wnt5a elevated the nuclear beta-catenin level in pancreatic cancer cells, without altering the Ror2 expression. Targeted reduction of beta-catenin antagonized exogenous Wnt5a-induced EMT and invasiveness in pancreatic cancer cells. CONCLUSION: Upregulation of Wnt5a promotes EMT and metastasis in pancreatic cancer models, which involves activation of beta-catenin-dependent canonical Wnt

signaling. These findings warrant further investigation of the clinical relevance of Wnt5 upregulation in pancreatic cancer.

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[353]

TÍTULO / TITLE: - Role of F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in diagnosis and management of pancreatic cancer; comparison with Multidetector Row Computed Tomography, Magnetic Resonance Imaging and Endoscopic Ultrasonography.

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

REVISTA / JOURNAL: - Rev Esp Med Nucl. Acceso gratuito al texto completo a partir de los 2 años de la fecha de publicación.

●● Enlace a la Editora de la Revista http://db.doyma.es/

●● Cita: Revista Española de Medicina Nuclear: <> Imagen Mol. 2013 Oct 16. pii: S2253-654X(13)00155-8. doi: 10.1016/j.remn.2013.08.005.

●● Enlace al texto completo (gratuito o de pago) 1016/j.remn.2013.08.005

AUTORES / AUTHORS: - Ergul N; Gundogan C; Tozlu M; Toprak H; Kadioglu H; Aydin M; Cermik TF

INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, Bezmialem Vakif University School of Medicine, Istanbul, Turkey. Electronic address: ngozubuyukoglu@gmail.com.

RESUMEN / SUMMARY: - OBJECTIVES: We aimed to analyze the contribution of 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) imaging to the diagnosis and management of pancreatic cancer compared with multidetector row computed tomography (MDCT), magnetic resonance imaging (MRI) and endoscopic ultrasonography (EUS). MATERIAL AND METHODS: We retrospectively scanned the data of 52 patients who were referred for FDG PET/CT imaging for evaluation of pancreatic lesions greater than 10mm. The diagnostic performances of 4 imaging methods and the impact of PET/CT on the management of pancreatic cancer were defined. RESULTS: Pancreatic adenocarcinoma was diagnosed in 33 of 52 patients (63%), 15 patients had benign diseases of pancreas (29%), and 4 patients were normal (8%). Sensitivity and NPV of EUS and PET/CT were equal (100%) and higher than MDCT and MRI. Specificity, PPV and NPV of PET/CT were significantly higher than MDCT. However, sensitivities of two imaging methods were not significantly different. There was no significant difference between PET/CT and MRI and EUS for these values. When the cut-off value of SUVmax was 3.2, the most effective sensitivity and specificity values were obtained. PET/CT contributed to the management of pancreatic cancer in 30% of patients. CONCLUSION: FDG PET/CT is a valuable imaging method for the diagnosis and management of pancreatic cancer, especially when applied along with EUS as first line diagnostic tools.

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[354]

TÍTULO / TITLE: - Association between ultraviolet radiation, skin sun sensitivity and risk of pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Epidemiol. 2013 Dec;37(6):886-92. doi: 10.1016/j.canep.2013.08.013. Epub 2013 Sep 26.

●● Enlace al texto completo (gratuito o de pago) 1016/j.canep.2013.08.013

AUTORES / AUTHORS: - Tran B; Whiteman DC; Webb PM; Fritschi L; Fawcett J; Risch HA; Lucas R; Pandeya N; Schulte A; Neale RE

INSTITUCIÓN / INSTITUTION: - Population Health Division, QIMR Berghofer Medical Research Institute, Australia; Centre for Research Excellence in Sun and Health, Australia. Electronic address: b.tran@uws.edu.au.

RESUMEN / SUMMARY: - Background: Ecological studies showing an inverse association between pancreatic cancer incidence and mortality and levels of ultraviolet radiation (UVR), suggest that higher levels of sun exposure may reduce risks of pancreatic cancer but there has been only one individual-level study that examined this issue. We aimed to examine the association between pancreatic cancer and markers of exposure to solar UVR, namely skin type, treatment of skin lesions, ambient UVR and time outdoors on work days. Methods: We used data from an Australian case-control study. Location at birth, residential location during adulthood, outdoors work, history of skin lesion treatment and sensitivity of the skin to the sun were obtained by questionnaire. We limited the analyses to Caucasians who answered the questionnaire about UVR (controls=589/711 recruited; cases=496/705 recruited). We used NASA's Total Ozone Mapping Spectrometer to estimate ambient UVR. Results: Being born in or living in areas of higher ambient UVR (compared to lower ambient UVR) was associated with about 30-40% lower risk of pancreatic cancer. People with fair skin colour had 47% lower risk of pancreatic cancer than those with dark skin colour (95% CI 0.37-0.75). There was some suggestion of increased risk with increased average number of hours spent outside at work. Conclusions: This study suggests that people with light skin colour or those born or living in areas of high ambient UVR have lower risk of pancreatic cancer. Our analysis supports an association between UVR and pancreatic cancer, possibly mediated through production of vitamin D.

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[355]

TÍTULO / TITLE: - Successful retreatment with chemoradiotherapy for local recurrence of pancreatic adenocarcinoma after neoadjuvant therapy and pancreaticoduodenectomy.

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

REVISTA / JOURNAL: - Gastrointest Cancer Res. 2013 Jul;6(4):118-9.

AUTORES / AUTHORS: - Gowarty MA; Zaki BI; Tsapakos MJ; Gordon SR; Suriawinata AA; Tsongalis GJ; Sutton JE; Pipas JM

INSTITUCIÓN / INSTITUTION: - Gastrointestinal Oncology Program Norris Cotton Cancer Center Dartmouth-Hitchcock Medical Center Lebanon, NH.

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[356]

TÍTULO / TITLE: - Risk factors of postoperative pancreatic fistula in curative gastric cancer surgery.

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

REVISTA / JOURNAL: - J Gastric Cancer. 2013 Sep;13(3):179-84. doi: 10.5230/jgc.2013.13.3.179. Epub 2013 Sep 30.

●● Enlace al texto completo (gratuito o de pago) 5230/jgc.2013.13.3.179

AUTORES / AUTHORS: - Yu HW; Jung do H; Son SY; Lee CM; Lee JH; Ahn SH; Park do J; Kim HH

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea.

RESUMEN / SUMMARY: - PURPOSE: Postoperative pancreatic fistula is a dreadful complication after gastric cancer surgery. The purpose of this study is to evaluate the actual incidence and risk factors of postoperative pancreatic fistula after curative gastrectomy for gastric cancer. MATERIALS AND METHODS: A total of 900 patients who underwent gastrectomy for gastric cancer (laparoscopic gastrectomy, 594 patients; open gastrectomy 306 patients) were enrolled between January 2009 and December 2010. Clinical outcomes, including postoperative pancreatic fistula grade based on the International Study Group on Pancreatic Fistula, were investigated. RESULTS: Overall, the postoperative pancreatic fistula rate was 3.3% (30/900) (1.5% in laparoscopic gastrectomy versus 6.9% in open gastrectomy, P<0.001). Patients who underwent D2 lymphadenectomy, total gastrectomy, splenectomy or distal pancreatectomy showed higher postoperative pancreatic fistula rates (4.7%, 13.8%, 13.6%, or 57.1%, respectively, P<0.001). Patients with postoperative pancreatic fistula had higher morbidity (46.7% versus 13.1%, P<0.001), delayed gas out (4.9 days versus 3.8 days, P<0.001), belated diet start (5.8 days versus 3.5 days, P<0.001) and longer postoperative hospital stay (13.7 days versus 6.8 days, P<0.001). On the multivariate analysis, total gastrectomy (odds ratio 9.751, 95% confidence interval: 3.348 to 28.397, P<0.001), distal pancreatectomy (odds ratio 7.637, 95% confidence interval: 1.668 to 34.961, P=0.009) and open gastrectomy (odds ratio 2.934, 95% confidence interval: 1.100 to 7.826, P=0.032) were the independent risk factors of postoperative pancreatic fistula. CONCLUSIONS: Laparoscopic gastrectomy had an advantage over open gastrectomy in terms of the lower postoperative pancreatic fistula rate. Total gastrectomy and combined resection, such as distal pancreatectomy, should be performed carefully to minimize postoperative pancreatic fistula in gastric cancer surgery.

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[357]

TÍTULO / TITLE: - Clinical necessity of the immunohistochemical reassessment of para-aortic lymph nodes in resected pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Oncol Lett. 2013 Nov;6(5):1189-1194. Epub 2013 Aug 21.

●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1539

AUTORES / AUTHORS: - Choi SH; Kim SH; Choi JJ; Kang CM; Hwang HK; Lee WJ

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Yonsei University College of Medicine, Seoul 120-752, South Korea ; Pancreaticobiliary Cancer Clinic, Institute of Gastroenterology, Severance Hospital, Seoul 120-752, South Korea.

RESUMEN / SUMMARY: - Para-aortic lymph node (PALN) metastasis is widely regarded as a systemic disease in cancer. Undetected PALN micrometastases during routine hematoxylin and eosin (HE) staining may be a cause of poor prognosis following a potentially curative pancreatectomy for pancreatic cancer. In the present study, paraffin-embedded PALN tissue blocks from 99 patients who underwent a pancreatectomy were re-evaluated by immunohistochemical staining using cytokeratin (CK)-19. Patients with PALN metastasis were summarized according to the clinicopathological data. A total of 484 PALNs (median, 4.9 nodes per patient; range, 1-19) were evaluated. PALN metastases were revealed in eight patients (8.1%) by routine HE staining of frozen section biopsies and in one patient (1.0%) by HE staining of a permanent section. Only one patient (1.0%) demonstrated micrometastasis by IHC; this patient did not display any adverse pathological characteristics and had a

relatively favorable survival period of 41 months. The present study concluded that an additional reassessment for micrometastasis in PALNs using CK-19 immunohistochemistry (IHC) is not a viable method for determining the survival outcome. A careful examination of a frozen section biopsy is sufficient for attempting curative surgery.

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[358]

TÍTULO / TITLE: - Clinical predictors of resectability of pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Saudi J Gastroenterol. 2013 Nov-Dec;19(6):278-85. doi: 10.4103/1319-3767.121036.

●● Enlace al texto completo (gratuito o de pago) 4103/1319-3767.121036

AUTORES / AUTHORS: - Almadi MA; Alharbi O; Azzam N; Altayeb M; Javed M; Alsaif F; Hassanain M; Alsharabi A; Al-Saleh K; Aljebreen AM

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology; Division of Gastroenterology and the Section of HPB, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia.

RESUMEN / SUMMARY: - Background/Aims: Identifying patient-related factors as well as symptoms and signs that can predict pancreatic cancer at a resectable stage, which could be used in an attempt to identify patients at an early stage of pancreatic cancer that would be appropriate for surgical resection and those at an unresectable stage be sparred unnecessary surgery. Materials and Methods: A retrospective chart review was conducted at a major tertiary care, university hospital in Riyadh, Saudi Arabia. The study population included individuals who underwent a computed tomography and a pancreatic mass was reported as well as the endoscopic reporting database of endoscopic procedures where the indication was a pancreatic mass, between April 1996 and April 2012. Any patient with a histologically confirmed diagnosis of adenocarcinoma of the pancreas was included in the analysis. We included patients' demographic information (age, gender), height, weight, body mass index, historical data (smoking, comorbidities), symptoms (abdominal pain and its duration, anorexia and its duration, weight loss and its amount, and over what duration, vomiting, abdominal distention, itching and its duration, change in bowel movements, change in urine color), jaundice and its duration. Other variables were also collected including laboratory values, location of the mass, the investigation undertaken, and the stage of the tumor. Results: A total of 61 patients were included, the mean age was 61.2 +/- 1.51 years, 25 (41%) were females. The tumors were located in the head (83.6%), body (10.9%), tail (1.8%), and in multiple locations (3.6%) of the pancreas. Half of the patients (50%) had Stage IV, 16.7% stages IIB and III, and only 8.3% were stages IB and IIA. On univariable analysis a lower hemoglobin level predicted resectability odds ratio 0.65 (95% confidence interval, 0.42-0.98), whereas on multivariable regression none of the variables included in the model could predict resectability of pancreatic cancer. A CA 19-9 cutoff level of 166 ng/mL had a sensitivity of 89%, specificity of 75%, positive likelihood ratio of 3.6, and a negative likelihood ratio of 0.15 for resectability of pancreatic adenocarcinoma. Conclusion: This study describes the clinical characteristics of patients with pancreatic adenocarcinoma in Saudi Arabia. None of the clinical or laboratory variables that were included in our study could independently predict resectability of pancreatic adenocarcinoma. Further studies are warranted to validate these results.

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[359]

TÍTULO / TITLE: - Analysis of risk factors for recurrence after curative resection of well-differentiated pancreatic neuroendocrine tumors based on the new grading classification.

ABABABA - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - J Hepatobiliary Pancreat Sci. 2013 Oct 20. doi: 10.1002/jhbp.47.

●● Enlace al texto completo (gratuito o de pago) 1002/jhbp.47

AUTORES / AUTHORS: - Tsutsumi K; Ohtsuka T; Fujino M; Nakashima H; Aishima S; Ueda J; Takahata S; Nakamura M; Oda Y; Tanaka M

INSTITUCIÓN / INSTITUTION: - Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Fukuoka, 812-8582, Japan.

ABABABA - BACKGROUND: It is difficult to predict the malignant potential of pancreatic neuroendocrine tumors (PNETs) precisely. This study investigated the validity of a new grading system adopted by the World Health Organization 2010 classification to determine risk factors for recurrence of PNETs. METHODS: Data of 70 patients with PNETs who underwent curative resection were retrospectively examined by uni- and multivariate analyses. Histopathological findings were re-reviewed by experienced pathologists. NET G1 was defined as mitotic count <2 per 10 high power fields (HPF) and/or </=2% Ki67 index, and NET G2 as 2-20 mitosis per 10 HPF and/or 3-20% Ki67 index. RESULTS: There were 58 patients with NET G1 and 12 with NET G2. Incidence of recurrence was 11.4%. Univariate analysis demonstrated significant risk factors for recurrence including NET G2 of histological grade (P = 0.0089), male gender (P = 0.0333), tumor size >/= 20 mm (P = 0.0117), lymph node metastasis (P = 0.0004), liver metastasis (P < 0.0001), lymphatic invasion (P = 0.046), and neural invasion (P = 0.0002). By multivariate analysis, histological grade (hazard ratio; 59.76, P = 0.0022) and neural invasion (hazard ratio; 147.49, P = 0.0016) were significantly associated with recurrence of PNETs. CONCLUSIONS: This study confirmed the prognostic relevance of the new grading classification and that evaluation of perineural invasion and histological grade should be considered as prognostic predictors in well-differentiated PNETs (NET G1 and G2).

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[360]

TÍTULO / TITLE: - Pancreatic cancer: practical strategies for early diagnosis and management.

ABABABA - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - JAAPA. 2013 Oct;26(10):27-32. doi: 10.1097/01.JAA.0000435004.09599.30.

●● Enlace al texto completo (gratuito o de pago) 1097/01.JAA.0000435004.09599.30

AUTORES / AUTHORS: - Tannery KM; Rizzolo D

INSTITUCIÓN / INSTITUTION: - Krista M. Tannery practices in the hospitalist medicine department, First Health Physicians Group, First Health of the Carolinas, at Moore Regional Hospital in Pinehurst, North Carolina. Denise Rizzolo is an associate professor in the PA program at Seton Hall University in South Orange, New Jersey, and a clinical assistant professor in the PA program at Pace University in New York

City. The authors have indicated no relationships to disclose relating to the content of this article.
ABABABA - Pancreatic cancer often is diagnosed too late for effective treatment. Knowing the risk factors, best diagnostic tests, and management options may help clinicians recognize pancreatic adenocarcinoma earlier, improving patient outcomes.

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[361]
TÍTULO / TITLE: - microRNA and gene networks in human pancreatic cancer.
ABABABA - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Oncol Lett. 2013 Oct;6(4):1133-1139. Epub 2013 Aug 9.
●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1521
AUTORES / AUTHORS: - Zhu M; Xu Z; Wang K; Wang N; Li Y
INSTITUCIÓN / INSTITUTION: - College of Computer Science and Technology, Jilin University, Changchun, Jilin 130012, P.R. China ; Key Laboratory of Symbolic Computation and Knowledge Engineering of the Ministry of Education, Jilin University, Changchun, Jilin 130012, P.R. China.
ABABABA - To date, scientists have obtained a substantial amount of knowledge with regard to genes and microRNAs (miRNAs) in pancreatic cancer (PC). However, deciphering the regulatory mechanism of these genes and miRNAs remains difficult. In the present study, three regulatory networks consisting of a differentially-expressed network, a related network and a global network, were constructed in order to identify the mechanisms and certain key miRNA and gene pathways in PC. The interactions between transcription factors (TFs) and miRNAs, miRNAs and target genes and an miRNA and its host gene were investigated. The present study compared and analyzed the similarities and differences between the three networks in order to distinguish the key pathways. Certain pathways involving the differentially-expressed genes and miRNAs demonstrated specific features. TP53 and hsa-miR-125b were observed to form a self-adaptation association. A further 16 significant differentially-expressed miRNAs were obtained and it was observed that an miRNA and its host gene exhibit specific features in PC, for example, hsa-miR-196a-1 and its host gene, HOXB7, form a self-adaptation association. The differentially-expressed network partially illuminated the mechanism of PC. The present study provides comprehensive data that is associated with PC and may aid future studies in obtaining pertinent data results with regards to PC. In the future, an improved understanding of PC may be obtained through an increased knowledge of the occurrence, mechanism, improvement, metastasis and treatment of the disease.

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[362]
TÍTULO / TITLE: - Autocrine extra-pancreatic trypsin 3 secretion promotes cell proliferation and survival in esophageal adenocarcinoma.
ABABABA - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Oct 11;8(10):e76667. doi: 10.1371/journal.pone.0076667.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0076667
AUTORES / AUTHORS: - Han S; Lee CW; Trevino JG; Hughes SJ; Sarosi GA Jr
INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Florida College of Medicine, Gainesville, Florida, United States of America.

ABABABA - Trypsin or Tumor associated trypsin (TAT) activation of Protease-activated receptor 2 (PAR-2) promotes tumor cell proliferation in gastrointestinal cancers. The role of the trypsin/PAR-2 network in esophageal adenocarcinoma (EA) development has not yet been investigated. The aim of this study is to investigate the role of trypsin/PAR-2 activation in EA tumorogenesis and therapy. We found that esophageal adenocarcinoma cells (EACs) and Barrett's Metaplasia (BART) expressed high levels of type 3 extra-pancreatic trypsinogen (PRSS3), a novel type of TAT. Activity of secreted trypsin was detected in cultured media from EA OE19 and OE33 cultures but not from BART culture. Surface PAR-2 expression in BART and EACs was confirmed by both flow cytometry and immunofluorescence. Trypsin induced cell proliferation (approximately 2 fold; P<0.01) in all tested cell lines at a concentration of 10 nM. Inhibition of PAR-2 activity in EACs via the PAR-2 antagonist ENMD (500 microM), anti-PAR2 antibody SAM-11 (2 microg/ml), or siRNA PAR-2 knockdown, reduced cell proliferation and increased apoptosis by up to 4 fold (P<0.01). Trypsin stimulation led to phosphorylation of ERK1/2, suggesting involvement of MAPK pathway in PAR-2 signal transduction. Inhibition of PAR-2 activation or siRNA PAR-2 knockdown in EACs prior to treatment with 5 FU reduced cell viability of EACs by an additional 30% (P<0.01) compared to chemotherapy alone. Our data suggest that extra-pancreatic trypsinogen 3 is produced by EACs and activates PAR-2 in an autocrine manner. PAR-2 activation increases cancer cell proliferation, and promotes cancer cell survival. Targeting the trypsin activated PAR-2 pathway in conjunction with current chemotherapeutic agents may be a viable therapeutic strategy in EA.

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[363]

TÍTULO / TITLE: - High SIRT1 expression is a negative prognosticator in pancreatic ductal adenocarcinoma.

ABABABA - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 2;13:450. doi: 10.1186/1471-2407-13-450.

●● Enlace al texto completo (gratuito o de pago) 1186/1471-2407-13-450

AUTORES / AUTHORS: - Stenzinger A; Endris V; Klauschen F; Sinn B; Lorenz K; Warth A; Goeppert B; Ehemann V; Muckenhuber A; Kamphues C; Bahra M; Neuhaus P; Weichert W

INSTITUCIÓN / INSTITUTION: - Institute of Pathology, and National Center for Tumor Diseases (NCT), University Hospital Heidelberg, Heidelberg, Germany. albrecht.stenzinger@med.uni-heidelberg.de.

ABABABA - BACKGROUND: Several lines of evidence indicate that Sirt1, a class III histone deacetylase (HDAC) is implicated in the initiation and progression of malignancies and thus gained attraction as druggable target. Since data on the role of Sirt1 in pancreatic ductal adenocarcinoma (PDAC) are sparse, we investigated the expression profile and prognostic significance of Sirt1 in vivo as well as cellular effects of Sirt1 inhibition in vitro. METHODS: Sirt1 expression was analyzed by immunohistochemistry in a large cohort of PDACs and correlated with clinicopathological and survival data. Furthermore, we investigated the impact of overexpression and small molecule inhibition on Sirt1 in pancreatic cancer cell culture models including combinatorial treatment with chemotherapy and EGFR-inhibition. Cellular events were measured quantitatively in real time and corroborated by conventional readouts including FACS analysis and MTT assays. RESULTS: We

detected nuclear Sirt1 expression in 36 (27.9%) of 129 PDACs. SIRT1 expression was significantly higher in poorly differentiated carcinomas. Strong SIRT1 expression was a significant predictor of poor survival both in univariate (p = 0.002) and multivariate (HR 1.65, p = 0.045) analysis. Accordingly, overexpression of Sirt1 led to increased cell viability, while small molecule inhibition led to a growth arrest in pancreatic cancer cells and impaired cell survival. This effect was even more pronounced in combinatorial regimens with gefitinib, but not in combination with gemcitabine. CONCLUSIONS: Sirt1 is an independent prognosticator in PDACs and plays an important role in pancreatic cancer cell growth, which can be levered out by small molecule inhibition. Our data warrant further studies on SIRT1 as a novel chemotherapeutic target in PDAC.

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[364]

TÍTULO / TITLE: - Utility of Serum CA19-9 Levels in the Diagnosis of Pancreatic Ductal Adenocarcinoma in an Endoscopic Ultrasound Referral Population.

ABABABA - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - J Gastrointest Cancer. 2013 Nov 24.

●● Enlace al texto completo (gratuito o de pago) 1007/s12029-013-9563-x

AUTORES / AUTHORS: - Parikh DA; Durbin-Johnson B; Urayama S

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology and Hepatology, Department of Internal Medicine, University of California, Davis Medical Center, 4150 V St. PSSB 3500, Sacramento, CA, 95817-1460, USA.

ABABABA - PURPOSE: Recent data suggest the use of carbohydrate antigen (CA) 19-9 as a potential marker in the early detection of pancreatic ductal adenocarcinoma (PDAC) when used in the appropriate clinical setting. Here, we assess the utility of CA19-9 in PDAC detection in a select population of pancreatic endoscopic ultrasound (EUS) referrals. METHODS: Retrospective review of an institutional EUS Pancreas Registry containing cases referred from November 2002 to November 2011 was completed for categorical analyses with CA19-9 level. A separate case-control study for the subset of non-elevated CA19-9 PDAC population was also performed to characterize the clinical features in this unique group of patients. RESULTS: Two hundred eighty-three patients had available CA19-9 data in the registry and were included in the study. Compared to the typical PDAC distribution, the proportion of patients with stage I disease was significantly higher in our registry population (P < 0.0001). Elevated CA19-9 levels most often reflected a diagnosis of PDAC relative to other pancreaticobiliary diagnoses. However, we observed that 15 % of patients with PDAC had normal CA19-9 levels. Clinical characteristics for this false-negative PDAC group compared to the true-positive group demonstrated a predilection for detection of cancer in the body/tail of the pancreas (P = 0.03), increased likelihood of lymph node metastases (P = 0.03), and initial presentation with vague abdominal pain or pancreatic mass as an incidental finding on imaging studies (P = 0.01). CONCLUSIONS: Elevated CA19-9 demonstrated a greater likelihood of PDAC diagnosis relative to benign pancreatic pathology, and higher levels of CA19-9 were in line with worse PDAC stage. Patients with normal CA19-9 PDAC may represent a unique subclass of patients, presenting with atypical clinical features, and possibly more advanced stage disease at the time of diagnosis. These patients may benefit from more diligent EUS examination or perhaps closer follow-up management.

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[365]

TÍTULO / TITLE: - Reduction of Decoy Receptor 3 Enhances TRAIL-Mediated Apoptosis in Pancreatic Cancer.
ABABABA - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Oct 25;8(10):e74272. doi: 10.1371/journal.pone.0074272.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0074272
AUTORES / AUTHORS: - Wang W; Zhang M; Sun W; Yang S; Su Y; Zhang H; Liu C; Li X; Lin L; Kim S; Okunieff P; Zhang Z; Zhang L
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Second Affiliated Hospital of Fujian Medical University, Quanzhou, Fujian, China.
ABABABA - Most human pancreatic cancer cells are resistant to tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL)-mediated apoptosis. However, the mechanisms by which pancreatic cancer cells utilize their extracellular molecules to counteract the proapoptotic signaling mediated by the TNF family are largely unknown. In this study, we demonstrate for the first time that DcR3, a secreted decoy receptor that malignant pancreatic cancer cells express at a high level, acts as an extracellular antiapoptotic molecule by binding to TRAIL and counteracting its death-promoting function. The reduction of DcR3 with siRNA unmasked TRAIL and greatly enhanced TRAIL-induced apoptosis. Gemcitabine, a first-line drug for pancreatic cancer, also reduced the level of DcR3. The addition of DcR3 siRNA further enhanced gemcitabine-induced apoptosis. Notably, our in vivo study demonstrated that the therapeutic effect of gemcitabine could be enhanced via further reduction of DcR3, suggesting that downregulation of DcR3 in tumor cells could tip the balance of pancreatic cells towards apoptosis and potentially serve as a new strategy for pancreatic cancer therapy.

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[366]
TÍTULO / TITLE: - Solid pseudopapillary neoplasm of the pancreas: a case report with review of the diagnostic dilemmas and tumor behavior.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Oman Med J. 2013 Nov;28(6):441-4. doi: 10.5001/omj.2013.122.
●● Enlace al texto completo (gratuito o de pago) 5001/omj.2013.122
AUTORES / AUTHORS: - Lakhtakia R; Al-Wahaibi K; Zahid KF; Malik KA; Burney IA
INSTITUCIÓN / INSTITUTION: - Head of Department, Department of Pathology, College of Medicine & Health Sciences, Sultan Qaboos University, Al Khoud, PO Box 35 P.C 123, Sultanate of Oman.
RESUMEN / SUMMARY: - Solid pseudopapillary neoplasm of the pancreas is a rare tumor of the pancreas often detected initially on imaging. Of uncertain histogenesis, it has a low-grade malignant potential with excellent post-surgical curative rates and rare metastasis. Despite advances in imaging, pseudocysts and other cystic neoplasms feature in the differential diagnosis. Pathological and/or cytological evaluation remains the gold standard in reaching a definitive diagnosis. On morphology alone, other primary pancreatic tumors and metastatic tumors pose a diagnostic challenge. Recent advances in immunohistochemical characterization have made the histopathologic diagnosis more specific and, in turn, shed light on the likely histogenesis of this rare tumor. We report a case of solid pseudopapillary neoplasm of the pancreas that was suspected on radiology and diagnosed intraoperatively on imprint cytology guiding definitive surgery. The diagnostic dilemmas are reviewed.

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[367]

TÍTULO / TITLE: - Case report of pancreatic dermoid cyst: can fine needle aspiration make the diagnosis?

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):653-6. doi: 10.6092/1590-8577/1787.

AUTORES / AUTHORS: - Lyons DA; Coberly EA; Hammoud GM; Nicholl MB

INSTITUCIÓN / INSTITUTION: - Division of Surgical Oncology, Department of Surgery, University of Missouri-Columbia. Columbia, MO, USA. dlyons9715@gmail.com.

RESUMEN / SUMMARY: - CONTEXT: Pancreatic dermoid cysts are rare, benign, germ cell tumors and part of the differential diagnosis for cystic neoplasms of the pancreas. CASE REPORT: A 35-year-old man presented with an incidentally discovered, 2 cm cystic pancreatic neoplasm of the pancreatic tail identified on CT scan. Endoscopic ultrasound (EUS) revealed a complex, honeycomb lesion. Fine needle aspiration (FNA) yielded a sample of whitish, necrotic material containing histiocytes, benign epithelial cells, and lymphocytes. After distal pancreatectomy and splenectomy was performed, histology revealed a cyst lined by stratified squamous epithelium with benign sebaceous units consistent with a pancreatic dermoid cysts. DISCUSSION: Although axial imaging reliably detects cystic neoplasms of the pancreas, diagnostic criteria for rare lesions are lacking; therefore alternative modalities such as EUS/FNA can be utilized. This case report highlights the EUS and FNA findings associated with pancreatic dermoid cysts.

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[368]

TÍTULO / TITLE: - Association between Helicobacter pylori Infection and Pancreatic Cancer Development: A Meta-Analysis.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 26;8(9):e75559. doi: 10.1371/journal.pone.0075559.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0075559

AUTORES / AUTHORS: - Xiao M; Wang Y; Gao Y

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, Wuxi People's Hospital of Nanjing Medical University, Wuxi, Jiangsu Province, China ; Second Department of Hepatobiliary Surgery, Zhujiang Hospital of Southern Medical University, Guangzhou, Guangdong Province, China.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is one of the most troublesome malignancies with dismal prognosis. H. pylori has been recognized as a type I carcinogen. Several studies have evaluated the association between H. pylori infection and pancreatic cancer development, however, the conclusions are inconsistent. METHODS: Literature search was carried out in PubMed, EMBASE, Cochrane Library and CNKI databases to identify eligible researches. We performed overall meta-analysis of all studies included and subgroup analysis based on regional distribution. Quality of the studies (assessed by Newcastle-Ottawa quality assessment scale for case-control studies) and CagA+ strains of H. pylori were taken into consideration, and we conducted additional analyses including high-quality researches and those concerning CagA+ H. pylori respectively. RESULTS: 9 studies involving 3033 subjects (1083 pancreatic cancer cases, 1950 controls) were included. Summary OR and 95%CI of the overall meta-analysis of all included studies were 1.47 and 1.22-

1.77, pooled data of the 4 high-quality studies were OR 1.28, 95%CI 1.01-1.63. OR of the 5 studies examined CagA+ strains was 1.42, corresponding 95%CI was 0.79 to 2.57. Summary estimates of subgroup analysis based on regional distribution are as follows, Europe group: OR 1.56, 95%CI 1.15-2.10; East Asia group: OR 2.01, 95%CI 1.33-3.02; North America group: OR 1.17, 95%CI 0.87-1.58. There was not obvious heterogeneity across the 9 studies. No publication bias was detected. CONCLUSION: H. pylori infection is significantly, albeit weakly, associated with pancreatic cancer development. The association is prominent in Europe and East Asia, but not in North America. CagA+ H. pylori strains appear not to be associated with pancreatic cancer. However, more studies, especially prospective studies, are needed to validate our results.

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[369]

TÍTULO / TITLE: - Provincial rates and time trends in pancreatic cancer outcomes.

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

REVISTA / JOURNAL: - Curr Oncol. 2013 Oct;20(5):279-81. doi: 10.3747/co.20.1672.

●● Enlace al texto completo (gratuito o de pago) 3747/co.20.1672

AUTORES / AUTHORS: - Fung S; Forte T; Rahal R; Niu J; Bryant H

INSTITUCIÓN / INSTITUTION: - Canadian Partnership Against Cancer, Toronto, ON.

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[370]

TÍTULO / TITLE: - Pathologic response with neoadjuvant chemotherapy and stereotactic body radiotherapy for borderline resectable and locally-advanced pancreatic cancer.

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

REVISTA / JOURNAL: - Radiat Oncol. 2013 Oct 31;8(1):254.

●● Enlace al texto completo (gratuito o de pago) 1186/1748-717X-8-254

AUTORES / AUTHORS: - Rajagopalan MS; Heron DE; Wegner RE; Zeh HJ; Bahary N; Krasinskas AM; Lembersky B; Brand R; Moser AJ; Quinn AE; Burton SA

RESUMEN / SUMMARY: - BACKGROUND: Neoadjuvant stereotactic body radiotherapy (SBRT) has potential applicability in the management of borderline resectable and locally-advanced pancreatic adenocarcinoma. In this series, we report the pathologic outcomes in the subset of patients who underwent surgery after neoadjuvant SBRT. METHODS: Patients with borderline resectable or locally-advanced pancreatic adenocarcinoma who were treated with SBRT followed by resection were included. Chemotherapy was to the discretion of the medical oncologist and preceded SBRT for most patients. RESULTS: Twelve patients met inclusion criteria. Most (92%) received neoadjuvant chemotherapy, and gemcitabine/capecitabine was most frequently utilized (n = 7). Most were treated with fractionated SBRT to 36 Gy/3 fractions (n = 7) and the remainder with single fraction to 24 Gy (n = 5). No grade 3+ acute toxicities attributable to SBRT were found. Two patients developed post-surgical vascular complications and one died secondary to this. The mean time to surgery after SBRT was 3.3 months. An R0 resection was performed in 92% of patients (n = 11/12). In 25% (n = 3/12) of patients, a complete pathologic response was achieved, and an additional 16.7% (n = 2/12) demonstrated <10% viable tumor cells. Kaplan-Meier estimated median progression free survival is 22.4 months. Overall survival is 92%, 64% and 51% at 1-, 2-, and 3-years. CONCLUSIONS: This study reports the pathologic response in patients treated with neoadjuvant chemotherapy and SBRT for

borderline resectable and locally-advanced pancreatic cancer. In our experience, 92% achieved an R0 resection and 41.7% of patients demonstrated either complete or extensive pathologic response to treatment. The results of a phase II study of this novel approach will be forthcoming.

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[371]

TÍTULO / TITLE: - CETN1 is a cancer testis antigen with expression in prostate and pancreatic cancers.

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

REVISTA / JOURNAL: - Biomark Res. 2013 Jun 13;1(1):22.

●● Enlace al texto completo (gratuito o de pago) 1186/2050-7771-1-22

AUTORES / AUTHORS: - Kim JJ; Rajagopalan K; Hussain B; Williams BH; Kulkarni P; Mooney SM

INSTITUCIÓN / INSTITUTION: - Department of Urology, James Buchanan Brady Urological Institute, The Johns Hopkins University, School of Medicine, Baltimore, MD, 21287, USA. smooney4@jhmi.edu.

RESUMEN / SUMMARY: - BACKGROUND: The Cancer Testis Antigens (CTAs) are a group of genes that are highly expressed in the normal testis and several types of cancer. Due to their restricted expression in normal adult tissues, CTAs have been attractive targets for immunotherapy and biomarker development. In this work, we discovered that Centrin 1 (CETN1) which is found in the centrosome of all eukaryotes, may be a member of this group and is highly expressed in prostate and pancreatic cancer. Three members of the centrin family of calcium binding proteins (CETN) are localized to the centrosome in all eukaryotes with CDC31 being the sole yeast homolog. CETN1 is a retrogene that probably arose from a retrotransposition of CETN2, an X-linked gene. A previous mouse study shows that CETN1 is expressed solely in the testis, while CETN2 is expressed in all organs. RESULTS: In this work, we show that CETN1 is a new member of the growing group of CTAs. Through the mining of publicly available microarray data, we discovered that human CETN1 expression but not CETN2 or CETN3 is restricted to the testis. In fact, CETN1 is actually down-regulated in testicular malignancies compared to normal testis. Using q-PCR, CETN1 expression is shown to be highly up-regulated in cancer of the prostate and in pancreatic xenografts. Unexpectedly however, CETN1 expression was virtually absent in various cell lines until they were treated with the DNA demethylation agent 5'AZA-2'Deoxycytidine (AZA) but showed no increased expression upon incubation with Histone deacetylase inhibitor Trichostatin-A (TSA) alone. Additionally, like most CTAs, CETN1 appears to be an intrinsically disordered protein which implies that it may occupy a hub position in key protein interaction networks in cancer. Neither CETN1 nor CETN2 could compensate for loss of CDC31 expression in yeast which is analogous to published data for CETN3. CONCLUSIONS: This work suggests that CETN1 is a novel CTA with expression in cancer of the prostate and pancreas. In cell lines, the expression is probably regulated by promoter methylation, while the method of regulation in normal adult tissues remains unknown.

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[372]

TÍTULO / TITLE: - Long-term effect of gemcitabine-combined endoscopic ultrasonography-guided brachytherapy in pancreatic cancer.

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

REVISTA / JOURNAL: - J Interv Gastroenterol. 2013 Jan;3(1):18-24.

●● Enlace al texto completo (gratuito o de pago) 7178/jig.102

AUTORES / AUTHORS: - Du Y; Jin Z; Meng H; Zou D; Chen J; Liu Y; Zhan X; Wang D; Liao Z; Li Z

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Changhai Hospital, the Second Military Medical University, Shanghai, China.

RESUMEN / SUMMARY: - BACKGROUND AND STUDY AIMS: Iodine 125 radioactive seeds implanted by endoscopic ultrasonography (EUS) represent a novel strategy for the treatment of pancreatic cancer. However, its long-term effects still remain unknown. The aim was to provide reliable data of long-term effects. Moreover, whether chemotherapy affects the result of EUS-guided implantation was also determined. PATIENTS AND METHODS: The present study prospectively observed 100 cases of unresectable pancreatic cancer underwent EUS-guided interstitial implantation of 125(I) radioactive seeds. Mean age was 60.9 years and 75% patients were staged III or IV. Eighty-five patients received routine gemcitabine-based chemotherapy one week after brachytherapy. The overall survival (OS) and progress-free survival (PFS) rates were evaluated for long-term effects. RESULTS: The mean follow-up time was 7.80+/-6.10 months (0.3-36 months), and the estimated median PFS and OS were 4.5 months (95% CI 3.1-5.9) and 7.0 months (95% CI 5.3-8.8), respectively. The estimated one-year and two-year survival rates were 21.0% and 4.0%. VAS scores dropped dramatically after one-week post implantation, and maintained significantly lower until the third month. Noticeably, there was no statistically difference on median survival time between cases with early and advanced cancer (8.6 vs. 6.0 months, p>0.05), nor between cases with or without previous chemotherapy (7.2 vs. 7.0 months, p>0.05). However, cases with post-implantation chemotherapy had a longer median survival as 7.8 months, compared with those untreated (4.0 months, p=0.003). CONCLUSIONS: Our data suggested EUS-guided radioactive seeds implantation an effective method to relieve pain in pancreatic cancer. However, no affirmative prolonged survival was observed and following chemotherapy was still necessary.

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[373]

TÍTULO / TITLE: - Nesidioblastosis and Pancreatic Non-functioning Islet Cell Tumor in an Adult with Type 2 Diabetes Mellitus.

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

REVISTA / JOURNAL: - Korean J Pathol. 2013 Oct;47(5):489-491. Epub 2013 Oct 25.

●● Enlace al texto completo (gratuito o de pago)

4132/KoreanJPathol.2013.47.5.489

AUTORES / AUTHORS: - Choi JE; Noh SJ; Sung JJ; Moon WS

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Research Institute for Endocrine Sciences and Research Institute of Clinical Medicine, Chonbuk National University Medical School, Jeonju, Korea.

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[374]

TÍTULO / TITLE: - Solid and cystic papillary neoplasm of the pancreas in a 18-year-old female: a case report.

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):642-5. doi: 10.6092/1590-8577/1410.

AUTORES / AUTHORS: - Fakhry H; Abdelhady H

INSTITUCIÓN / INSTITUTION: - Department of Surgical Oncology, South Egypt Cancer Institute, Assiut University. Assiut, Egypt. hussein_hozayen@yahoo.com.
RESUMEN / SUMMARY: - CONTEXT: Solid and cystic papillary neoplasm of the pancreas is an extremely rare neoplasm that mostly affects young females in the mean age of 25 years and accounts for about 0.2-2.7% of all pancreatic tumors. CASE REPORT: A 18-year-old female presented with progressively increasing mass in the left hypochondrium and epigastric regions and vague abdominal pain. There was no history of jaundice and vomiting. The mean diameter of the tumors was 17x24 cm. Preoperative core needle revealed solid and cystic papillary neoplasm. Distal pancreatectomy and splenectomy were performed. The patient did not receive adjuvant therapy and no tumor recurrence was detected in follow up. CONCLUSION: Solid and cystic papillary neoplasm may reach large dimensions with a benign behavior and is curable by surgical excision. Differential diagnosis from other tumors with aggressive behavior is therefore important.

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[375]
TÍTULO / TITLE: - MUC1 Regulates Expression of Multiple microRNAs Involved in Pancreatic Tumor Progression, Including the miR-200c/141 Cluster.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Oct 15;8(10):e73306. doi: 10.1371/journal.pone.0073306.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0073306
AUTORES / AUTHORS: - Mohr AM; Bailey JM; Lewallen ME; Liu X; Radhakrishnan P; Yu F; Tapprich W; Hollingsworth MA
INSTITUCIÓN / INSTITUTION: - Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, Nebraska, United States of America.
RESUMEN / SUMMARY: - MUC1 is a transmembrane glycoprotein that modulates transcription via its cytoplasmic domain. We evaluated the capacity of MUC1 to regulate the global transcription of microRNAs in pancreatic cancer cells expressing MUC1. Results indicated that MUC1 regulated expression of at least 103 microRNAs. We evaluated further regulation of the microRNA transcript cluster miR-200c/141, which was among the most highly regulated microRNAs. We found that MUC1 directly interacted with ZEB1, a known transcriptional repressor of the miR-200c/141 cluster, at the promoter of miR-200c/141, and further reduced transcript production. These data indicate that signaling through MUC1 influences cancer progression by regulating transcription of microRNAs that are associated with the process of metastasis.

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[376]
TÍTULO / TITLE: - MicroRNA-200c Modulates the Expression of MUC4 and MUC16 by Directly Targeting Their Coding Sequences in Human Pancreatic Cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Oct 25;8(10):e73356. doi: 10.1371/journal.pone.0073356.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0073356
AUTORES / AUTHORS: - Radhakrishnan P; Mohr AM; Grandgenett PM; Steele MM; Batra SK; Hollingsworth MA

INSTITUCIÓN / INSTITUTION: - Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, Nebraska, United States of America.

RESUMEN / SUMMARY: - Transmembrane mucins, MUC4 and MUC16 are associated with tumor progression and metastatic potential in human pancreatic adenocarcinoma. We discovered that miR-200c interacts with specific sequences within the coding sequence of MUC4 and MUC16 mRNAs, and evaluated the regulatory nature of this association. Pancreatic cancer cell lines S2.028 and T3M-4 transfected with miR-200c showed a 4.18 and 8.50 fold down regulation of MUC4 mRNA, and 4.68 and 4.82 fold down regulation of MUC16 mRNA compared to mock-transfected cells, respectively. A significant reduction of glycoprotein expression was also observed. These results indicate that miR-200c overexpression regulates MUC4 and MUC16 mucins in pancreatic cancer cells by directly targeting the mRNA coding sequence of each, resulting in reduced levels of MUC4 and MUC16 mRNA and protein. These data suggest that, in addition to regulating proteins that modulate EMT, miR-200c influences expression of cell surface mucins in pancreatic cancer.

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[377]

TÍTULO / TITLE: - Expression of aldo-keto reductase family 1 member C3 (AKR1C3) in neuroendocrine tumors & adenocarcinomas of pancreas, gastrointestinal tract, and lung.

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

REVISTA / JOURNAL: - Int J Clin Exp Pathol. 2013 Oct 15;6(11):2419-29.

AUTORES / AUTHORS: - Chang TS; Lin HK; Rogers KA; Brame LS; Yeh MM; Yang Q; Fung KM

INSTITUCIÓN / INSTITUTION: - Department of Pathology, University of Oklahoma Health Sciences Center Oklahoma City, OK.

RESUMEN / SUMMARY: - Human aldo-keto reductase family 1 member C3 (AKR1C3) was initially identified as an enzyme in reducing 5alpha-dihydrotestosterone (5alpha-DHT) to 5alpha-androstane-3alpha, 17beta-diol (3alpha-diol) and oxidizing 3alpha-diol to androsterone. It was subsequently demonstrated to possess ketosteroid reductase activity in metabolizing other steroids including estrogen and progesterone, 11-ketoprostaglandin reductase activity in metabolizing prostaglandins, and dihydrodiol dehydrogenase x (DDx) activity in metabolizing xenobiotics. AKR1C3 was demonstrated in sex hormone-dependent tissues including testis, breast, endometrium, and prostate; in sex hormone-independent tissues including kidney and urothelium. Our previous study described the expression of AKR1C3 in squamous cell carcinoma and adenocarcinoma but not in small cell carcinoma. In this report, we studied the expression of AKR1C3 in normal tissue, adenocarcinomas (43 cases) and neuroendocrine (NE) tumors (40 cases) arising from the aerodigestive tract and pancreas. We demonstrated wide expression of AKR1C3 in superficially located mucosal cells, but not in NE cells. AKR1C3-positive immunoreactivity was detected in 38 cases (88.4%) of adenocarcinoma, but only in 7 cases (17.5%) of NE tumors in all cases. All NE tumors arising from the pancreas and appendix and most tumors from the colon and lung were negative. The highest ratio of positive AKR1C3 in NE tumors was found in tumors arising from the small intestine (50%). These results raise the question of AKR1C3's role in the biology of normal mucosal epithelia and tumors. In

addition, AKR1C3 may be a useful adjunct marker for the exclusion of the NE phenotype in diagnostic pathology.

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[378]

TÍTULO / TITLE: - Cytoplasmic expression of LGR5 in pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Front Physiol. 2013 Sep 26;4:269. doi: 10.3389/fphys.2013.00269.

●● Enlace al texto completo (gratuito o de pago) 3389/fphys.2013.00269

AUTORES / AUTHORS: - Mizuno N; Yatabe Y; Hara K; Hijioka S; Imaoka H; Shimizu Y; Ko SB; Yamao K

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Aichi Cancer Center Hospital Nagoya, Japan.

RESUMEN / SUMMARY: - Background: CD133 has been identified as a cancer stem cell marker for pancreatic ductal adenocarcinoma. Although leucine-rich-repeat-containing G-protein-coupled receptor 5 (LGR5), a marker of intestinal stem cells, has been shown to be on a higher level of the stem cell hierarchy than CD133, the expression and function of LGR5 in pancreatic cancer tissue remains unclear. This study investigated tissue expression of LGR5 and CD133 in resected pancreatic cancer tissue. Methods: LGR5 and CD133 expression was immunohistochemically examined in 9 patients with pancreatic ductal adenocarcinoma who underwent resection. Results: LGR5 was expressed in the cytoplasm of pancreatic cancer cells in 4 of 9 cases. CD133 was not detected in cancerous tissue. In non-neoplastic tissue, LGR5 was expressed in the basolateral membrane of a subset of endocrine cells. Conversely, CD133 was expressed in the apical membrane of small duct cells. Co-localization of LGR5 and CD133 was not found in either neoplastic or non-neoplastic tissue. LGR5 expression in pancreatic cancer cells showed no statistically significant correlation with survival after surgery. Conclusion: We have demonstrated that LGR5 is expressed in the cytoplasm of pancreatic adenocarcinoma cells, and the basolateral membrane of a subset of endocrine cells of the human pancreas. Further investigation is required to clarify any prognostic significance of LGR5 expression.

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[379]

TÍTULO / TITLE: - Two-wave nanotherapy to target the stroma and optimize gemcitabine delivery to a human pancreatic cancer model in mice.

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

REVISTA / JOURNAL: - ACS Nano. 2013 Nov 26;7(11):10048-65. doi: 10.1021/nn404083m. Epub 2013 Oct 28.

●● Enlace al texto completo (gratuito o de pago) 1021/nn404083m

AUTORES / AUTHORS: - Meng H; Zhao Y; Dong J; Xue M; Lin YS; Ji Z; Mai WX; Zhang H; Chang CH; Brinker CJ; Zink JI; Nel AE

INSTITUCIÓN / INSTITUTION: - Division of NanoMedicine, Department of Medicine, double daggerDepartment of Chemistry & Biochemistry, and section signCalifornia NanoSystems Institute, University of California , Los Angeles, California 90095, United States.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) elicits a dense stromal response that blocks vascular access because of pericyte coverage of vascular fenestrations. In this way, the PDAC stroma contributes to chemotherapy resistance in

addition to causing other problems. In order to improve the delivery of gemcitabine, a first-line chemotherapeutic agent, a PEGylated drug-carrying liposome was developed, using a transmembrane ammonium sulfate gradient to encapsulate the protonated drug up to 20% w/w. However, because the liposome was precluded from entering the xenograft site due to the stromal interference, we developed a first-wave nanocarrier that decreases pericyte coverage of the vasculature through interference in the pericyte recruiting TGF-beta signaling pathway. This was accomplished using a polyethyleneimine (PEI)/polyethylene glycol (PEG)-coated mesoporous silica nanoparticle (MSNP) for molecular complexation to a small molecule TGF-beta inhibitor, LY364947. LY364947 contains a nitrogen atom that attaches, through H-bonding, to PEI amines with a high rate of efficiency. The copolymer coating also facilitates systemic biodistribution and retention at the tumor site. Because of the high loading capacity and pH-dependent LY364947 release from the MSNPs, we achieved rapid entry of IV-injected liposomes and MSNPs at the PDAC tumor site. This two-wave approach provided effective shrinkage of the tumor xenografts beyond 25 days, compared to the treatment with free drug or gemcitabine-loaded liposomes only. Not only does this approach overcome stromal resistance to drug delivery in PDAC, but it also introduces the concept of using a stepwise engineered approach to address a range of biological impediments that interfere in nanocancer therapy in a spectrum of cancers.

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[380]

TÍTULO / TITLE: - A Novel Regulatory Mechanism of Pim-3 Kinase Stability and its Involvement in Pancreatic Cancer Progression.

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

REVISTA / JOURNAL: - Mol Cancer Res. 2013 Oct 28.

●● Enlace al texto completo (gratuito o de pago) 1158/1541-7786.MCR-13-0389

AUTORES / AUTHORS: - Zhang F; Liu B; Wang Z; Yu XJ; Ni QX; Yang WT; Mukaida N; Li YY

INSTITUCIÓN / INSTITUTION: - Fudan University Shanghai Cancer Center.

RESUMEN / SUMMARY: - Translationally-controlled tumor protein (TCTP/TPT1) was identified from a yeast two-hybrid screen and shown to interact with Pim-3, a member of the proto-oncogene Pim family with serine/threonine kinase activity. TCTP was aberrantly expressed in human pancreatic cancer cells and malignant ductal epithelial cells, but not in normal pancreatic duct epithelial cells adjacent to tumor foci of human pancreatic cancer tissue. Moreover, TCTP co-localized with Pim-3 both in human pancreatic cancer cells and clinical tissues. Mapping studies revealed that the interaction between Pim-3 and TCTP occurred through the C-terminal region of Pim-3 and N-terminal region of TCTP. Although Pim-3 had no effect on TCTP expression or phosphorylation, overexpression of TCTP increased the amount of Pim-3 in a dose-dependent manner. Interestingly, RNAi-mediated ablation of TCTP expression reduced Pim-3 protein but not mRNA, through a mechanism involving the ubiquitin-proteasome degradation system. As a consequence of Pim-3 instability and subsequent degradation, tumor growth in vitro and in vivo was inhibited by arresting cell cycle progression and enhancing apoptosis. Furthermore, TCTP and Pim-3 expression were significantly correlated in pancreatic adenocarcinoma specimens, and patients with highly expressed TCTP and Pim-3 presented with a more advanced tumor stage.

These observations indicate that TCTP enhances Pim-3 stability to simultaneously promote and prevent cell cycle progression and apoptosis, respectively. Hence, TCTP and Pim-3 serve a pivotal role in human pancreatic cancer with important ramifications for clinical diagnostic and therapeutic implications. Implications: The present study provides a new idea and experimental evidence for recognizing TCTP/Pim-3 pathway as a target for therapy in human pancreatic cancer.

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[381]

TÍTULO / TITLE: - Solid pseudo-papillary tumor of pancreas: A rare case report and review of Indian literature.

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

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Jul-Sep;9(3):507-10. doi: 10.4103/0973-1482.119364.

●● Enlace al texto completo (gratuito o de pago) 4103/0973-1482.119364

AUTORES / AUTHORS: - Murhekar K; Ramakrishnan AS; Ramani B; Sunil BJ; Majhi U

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Cancer Institute (WIA), Adyar, Chennai, India.

RESUMEN / SUMMARY: - Solid pseudo-papillary tumor (SPT) of the pancreas is a rare pancreatic tumor, well known for its predilection for young women. As the tumor has favorable prognosis, differentiating it from other pancreatic tumors with aggressive behavior is necessary. We present a rare case of SPT and review the literature about SPT cases published from India.

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[382]

TÍTULO / TITLE: - Pancreatic adenocarcinoma presenting as mandibular tumor: case report.

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

REVISTA / JOURNAL: - Oral Surg Oral Med Oral Pathol Oral Radiol. 2013 Oct 31. pii: S2212-4403(13)00427-6. doi: 10.1016/j.oooo.2013.08.009.

●● Enlace al texto completo (gratuito o de pago) 1016/j.oooo.2013.08.009

AUTORES / AUTHORS: - Jaffa NR; Adam D; Akhtar S; Kyzas PA

INSTITUCIÓN / INSTITUTION: - Senior House Officer, Department of Oral and Maxillofacial Surgery, Royal Preston Hospital, Lancashire Teaching Hospital Trust.

RESUMEN / SUMMARY: - CONTEXT: Pancreatic adenocarcinoma metastasizing to the mandible is extremely rare, with only 4 previous cases reported in the literature. Here, we present a patient with a metastatic lesion in the mandible as the initial manifestation of pancreatic adenocarcinoma. We also review the incidence, diagnosis, and management of this rare occurrence. CASE REPORT: A 45-year-old man with a 5-week history of pain, following a tooth extraction, was referred to our Oral & Maxillofacial Department and presented with a nonhealing socket in the mandibular premolar region. He was investigated by use of imaging and an urgent biopsy. The diagnosis of pancreatic neoplasm was made. At this stage, the disease was fairly extensive and management was palliative. CONCLUSION: This case demonstrates the importance of a full investigation when a patient presents with a nonhealing socket and pain after tooth extraction. Mandibular metastases from distant primaries often have poor prognosis, with most patients getting palliative support. A multidisciplinary team approach is required for the management of these rare cases.

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[383]
TÍTULO / TITLE: - Metastatic Merkel cell carcinoma (MCC) of pancreas and breast: a unique case.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - World J Surg Oncol. 2013 Oct 7;11(1):261. doi: 10.1186/1477-7819-11-261.
●● Enlace al texto completo (gratuito o de pago) 1186/1477-7819-11-261
AUTORES / AUTHORS: - Vernadakis S; Moris D; Bankfalvi A; Makris N; Sotiropoulos GC
INSTITUCIÓN / INSTITUTION: - Department of General, Visceral and Transplantation Surgery, University Hospital Essen, Hufelandstr, 55, Esse 45122, Germany. svernadakis@yahoo.com.
RESUMEN / SUMMARY: - Merkel cell carcinoma (MCC) is a rare potentially fatal skin tumor affecting older and immunosuppressed individuals. It is highly malignant with high rates of metastasis and poor survival.We present a case of a 67-year-old woman with a palpable mass in the upper abdomen. An abdominal CT revealed a mass in the tail of the pancreas. Two weeks before, lumpectomy of a 3.5 cm tumor of the left breast had been performed. Histology showed a primary neuroendocrine carcinoma of the mammary gland. The patient's medical history was significant for a 0.7 x 0.9 cm MCC removed from her left forearm 2.5 years ago. There was no evidence of vascular involvement or peritoneal disease and by all criteria was resectable. A somatostatin receptor scintigraphy showed an enhanced uptake in the pancreatic tail region. The tumor was immunohistochemically strong staining for synaptophysin and CD56. The diagnosis of a metastatic-MCC in the tail of the pancreas was made. Further histological investigation of the prior removed neuroendocrine breast tumor and the MCC of the left forearm confirmed neuroendocrine origin and identical histology to the previously resected MCC of the left forearm. In this article, we aim to highlight that MCC has the potential to spread even in unusual organs, such as pancreas or breast, and therefore a diligent follow-up should be applied in patients with MCC.

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[384]
TÍTULO / TITLE: - Contribution of endosonography in an uncommon case of pancreatic cysts.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - World J Gastrointest Endosc. 2013 Oct 16;5(10):519-22. doi: 10.4253/wjge.v5.i10.519.
●● Enlace al texto completo (gratuito o de pago) 4253/wjge.v5.i10.519
AUTORES / AUTHORS: - Sousa AL; Sousa D; Figueiredo P; Marques PP; Guerreiro H
INSTITUCIÓN / INSTITUTION: - Ana Lucia Sousa, Diamantino Sousa, Horacio Guerreiro, Department of Gastroenterology, Hospital de Faro E.P.E., 8000-386 Faro, Portugal.
RESUMEN / SUMMARY: - Here we present the case of a 35-year-old female patient with long standing dyspepsia and imaging studies showing the presence of multiple cysts in the head and tail of the pancreas. The patient underwent endosonography that confirmed the presence of multiple simple cysts throughout the entirety of the pancreas without dilation of the pancreatic duct. The majority of the cysts were less than one centimeter in size, and the largest cyst showed a honeycomb appearance. Cytology of aspirates from the two largest cysts was compatible with benign pancreatic cysts.

Endosonography also revealed cysts within the left kidney and spleen. Genetic testing confirmed Von Hippel-Lindau disease. We highlight this case because it is unusual for Von Hippel-Lindau disease, a rare clinical entity, to present solely with cysts in the absence of more common manifestations, such as hemangioblastomas in the central nervous system and malignancy.

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[385]

TÍTULO / TITLE: - Two rare cases of a solid pseudopapillary neoplasm of the pancreas.

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

REVISTA / JOURNAL: - Oncol Lett. 2013 Oct;6(4):871-874. Epub 2013 Jul 19.

●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1476

AUTORES / AUTHORS: - Saigo C; Hirose Y; Asano N; Takamatsu M; Fukushima N; Yasuda I; Goshima S; Ozeki M; Osada S

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Gifu University Hospital, Gifu 501-1194, Japan.

RESUMEN / SUMMARY: - A solid pseudopapillary neoplasm (SPN) of the pancreas has distinct histopathological features. A solid pattern of growth with pseudopapillary structures that result from degeneration is observed. On rare occasions, the tumor may vary from being entirely solid to completely cystic. The present study describes two unique cases of SPN. A 25-year-old male presented with a pancreatic tumor showing a predominantly solid pattern with no degenerative change, although the pre-operative cytological specimens that were obtained by endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) revealed pseudopapillary structures. The second case was of an 11-year-old female who presented with a pancreatic tumor with prominent degeneration. Nests and cords of the remaining neoplastic cells were located only at the periphery, with perineural invasion. An immunohistochemical analysis revealed that the tumor cells in the two cases were positive for CD10 and beta-catenin and negative for trypsin. An awareness of the broad morphological variability of SPN and an immunohistochemical panel that includes CD10, beta-catenin and trypsin are useful for establishing an accurate diagnosis.

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[386]

TÍTULO / TITLE: - Solid Pseudopapillary Neoplasm of the Pancreas: Report of a Rare Case and Review of the Literature.

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

REVISTA / JOURNAL: - Turk Patoloji Derg. 2013 Sep 24. doi: 10.5146/tjpath.2013.01192.

●● Enlace al texto completo (gratuito o de pago) 5146/tjpath.2013.01192

AUTORES / AUTHORS: - Yener AN; Manukyan M; Midi A; Cubuk R

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Maltepe University, Faculty of Medicine, ISTANBUL, TURKEY.

RESUMEN / SUMMARY: - Solid pseudopapillary neoplasm, a rare primary neoplasm of the pancreas that typically affects young women, is a relatively indolent entity with favorable prognosis. We here report a 20-year-old young girl with solid pseudopapillary neoplasm who presented with mild dull abdominal discomfort without any significant laboratory findings. On MRI, a heterogenous mass was found at the distal pancreas. The patient underwent en-block distal pancreatectomy with splenectomy with the presumptive diagnosis of cystic neoplasm of the pancreas. The tumor was well-

circumscribed, encapsulated, 5.5 cm in the greatest dimension and showed typical papillary and pseudopapillary structures. Capsular invasion was seen on focal areas. The patient was not given any adjuvant therapy and shows no sign of disease after six months follow-up. It is important to differentiate this tumor from other pancreatic neoplasms because this neoplasm is amenable to cure after complete surgical resection even in cases with capsular invasion, unlike malignant tumors of the pancreas.

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[387]

TÍTULO / TITLE: - Unexpected pheochromocytoma presenting as a pancreatic tumor: A case report.

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

REVISTA / JOURNAL: - Oncol Lett. 2013 Sep;6(3):833-834. Epub 2013 Jul 8.

●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1447

AUTORES / AUTHORS: - Huang YH; Liaw WJ; Kuo CP; Wu ZF; Cherng CH; Yu JC; Horng HC; Huang ST

INSTITUCIÓN / INSTITUTION: - Department of Anesthesiology, Tri-Service General Hospital and National Defense Medical Center, Taipei 11490, Taiwan, R.O.C.

RESUMEN / SUMMARY: - A 54-year-old female presented with a large pancreatic tumor of the tail during a regular physical examination. The patient underwent surgical intervention and the surgeon identified that the tumor originated from the retroperitoneal region. Markedly severe hemodynamic fluctuations occurred during the manipulation of the tumor and continued to occur subsequent to the tumor being removed. The vital signs were adequately managed and the surgery was successful without complications. The patient was discharged without any sequelae days later. The pathology report indicated a diagnosis of pheochromocytoma. Unexpected pheochromocytoma may lead to a fatal hypertensive crisis with catastrophic sequelae during surgery. The peri-operative management of pheochromocytoma remains a complicated challenge that requires intensive pre-operative preparation and vigilant peri-operative care. For surgeons and anesthesiologists who may encounter an unexpected hypertensive crisis during abdominal tumor surgery, undiagnosed pheochromocytoma should always be considered.

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[388]

TÍTULO / TITLE: - Solid pseudopapillary tumor of pancreas with sickle cell trait: a rare case report.

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

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Jul-Sep;9(3):537-40. doi: 10.4103/0973-1482.119363.

●● Enlace al texto completo (gratuito o de pago) 4103/0973-1482.119363

AUTORES / AUTHORS: - Permi HS; Kishan Prasad HL; Shetty BN; Rai BP; Raghuraja U; Bhat S

INSTITUCIÓN / INSTITUTION: - Department of Pathology, K S Hegde Medical Academy, Deralakatte, Mangalore, India.

RESUMEN / SUMMARY: - Solid pseudopapillary tumor of pancreas is a rare pancreatic neoplasm affecting young women, has low malignant potential and amenable for surgical excision with good long-term survival. Sickle cell trait is benign condition, which involves one normal beta-globin chain and one HbS chain. Although it is a

benign condition, individuals are prone to have rare complications that may predispose to death under certain circumstances. We report a rare coexistence of solid pseudopapillary tumor of pancreas with sickle cell trait in an 18-year-old female who underwent distal pancreatectomy with splenectomy. Histopathological examination and haemoglobin electrophoresis confirmed the diagnosis.

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[389]

TÍTULO / TITLE: - Differential Diagnosis of Focal Non-Cystic Pancreatic Lesions With and Without Proximal Dilation of Pancreatic Duct Noted on CT Scan.

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

REVISTA / JOURNAL: - Clin Transl Gastroenterol. 2013 Nov 7;4:e42. doi: 10.1038/ctg.2013.15.

●● Enlace al texto completo (gratuito o de pago) 1038/ctg.2013.15

AUTORES / AUTHORS: - Tummala Md P; Rao Md S; Agarwal Md B

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology and Hepatology, Saint Louis University School of Medicine, St Louis, Missouri, USA.

RESUMEN / SUMMARY: - OBJECTIVES: Pancreatic duct (PD) dilation proximal to a solid focal pancreatic lesion on computed tomography (CT) scan is considered highly suggestive of pancreatic adenocarcinoma. There is, however, no published data on the differential diagnosis of focal non-cystic pancreatic lesions with and without PD dilation. We assessed the diagnostic utility of this radiologic finding. METHODS: This is a retrospective analysis of a prospectively maintained database of university-based clinical practice. A total of 445 non-jaundiced patients who underwent endoscopic ultrasound (EUS) (2002-2010) for evaluation of solid pancreatic lesions noted on CT scan were included. Final diagnosis was based on surgical pathology or definitive cytology with supporting clinical follow-up of >/=12 months. Main outcome measurements included (1) differential diagnoses and (2) performance characteristics of EUS-fine needle aspiration (FNA) for diagnosing neoplasm in patients with non-cystic pancreatic lesions with and without PD dilation. RESULTS: A neoplasm was finally diagnosed in 152 of 187 patients with and 87 of 258 patients without PD dilation on CT scan. Chronic pancreatitis (diffuse and focal) was the predominant non-malignant diagnosis in patients with PD dilation. In patients without PD dilation, malignant lesions included neuroendocrine tumor, adenocarcinoma, metastasis, PEComa (perivascular epitheloid cell tumor), and lymphoma; and the non-neoplastic diagnosis included chronic pancreatitis, intrapancreatic lymph nodes, and infected pancreatic fluid collection. EUS-FNA had 97.6% accuracy for diagnosing a neoplasm in these patients. CONCLUSIONS: Dilation PD proximal to a focal solid pancreatic lesion increases the likelihood of malignancy but the performance characteristics of this radiologic finding are probably inadequate to guide clinical management. Neoplasms without dilated PD often require immunostaining for a definitive diagnosis.

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[390]

TÍTULO / TITLE: - Modified GTX as Second-Line Chemotherapy in Advanced Pancreatic Cancer.

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

REVISTA / JOURNAL: - Gastrointest Cancer Res. 2013 Jul;6(4):115-7.

AUTORES / AUTHORS: - Dbouk H; Ajouz H; Shamseddine A; Mukherji D; O'Reilly EM; Haydar A; Kelsen D; Naghy M; Eloubeidi M; Geara F; Saltz L; Abou-Alfa GK

INSTITUCIÓN / INSTITUTION: - American University of Beirut Beirut, Lebanon.

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[391]

TÍTULO / TITLE: - Accuracy of CA 19-9 and Radiologic Imaging in Detecting Recurrence After Resection for Pancreatic Cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):680-1. doi: 10.6092/1590-8577/1886.

AUTORES / AUTHORS: - Sperti C; Beltrame V; Bissoli S; Pedrazzoli S

INSTITUCIÓN / INSTITUTION: - Third Surgical Clinic, Department of Surgery, Oncology and Gastroenterology, University of Padua. Padua, Italy. csperti@libero.it.

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[392]

TÍTULO / TITLE: - Peripancreatic cystic lymphangioma diagnosed by endoscopic ultrasound/fine-needle aspiration: a rare mesenchymal tumour.

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

●● Cita: British Medical J. (BMJ): <> Case Rep. 2013 Oct 3;2013. pii: bcr2013200210. doi: 10.1136/bcr-2013-200210.

●● Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-200210

AUTORES / AUTHORS: - Tanimu S; Rafiullah; Resnick J; Onitilo AA

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Marshfield Clinic Weston Center, Weston, Wisconsin, USA.

RESUMEN / SUMMARY: - A 73-year-old man presented with a 5-month history of intermittent nausea, vomiting, central abdominal discomfort and a 17-pound weight loss over the past year. Laboratory testing, including a complete blood count with differential, liver function testing, amylase and lipase studies were normal. A CT scan showed a bilobed cystic lesion inferior to the body of the pancreas. An endoscopic ultrasound revealed a 5.3x3.9 cm, anechoic, bilobed cystic lesion, extrinsic to the body of the pancreas with a 1-2 mm septation and a normal pancreas. Fine-needle aspiration revealed a milky-white aspirate with negative cytology. Laboratory assessment of the cystic aspirant revealed carcinoembryonic antigen 1.7 ng/mL, amylase 148 units/L, cholesterol 300 mg/dL, and carbohydrate antigen 19-9 3 units/mL. He underwent resection of the mass, with the histopathology confirming a diagnosis of peripancreatic lymphangioma. He did well after the surgery with interval resolution of his symptoms.

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[393]

TÍTULO / TITLE: - Recognition of complications after pancreaticoduodenectomy for cancer determines inpatient mortality.

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):626-31. doi: 10.6092/1590-8577/1883.

AUTORES / AUTHORS: - Glazer ES; Amini A; Jie T; Gruessner RW; Krouse RS; Ong ES

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The University of Arizona. Tucson, AZ, USA. eglazer@email.arizona.edu.

RESUMEN / SUMMARY: - CONTEXT: While perioperative mortality after pancreaticoduodenectomy is decreasing, key factors remain to be elucidated.

OBJECTIVE: The purpose of this study was to investigate inpatient mortality after pancreaticoduodenectomy in the Nationwide Inpatient Sample (NIS), a representative inpatient database in the USA. METHODS: Patient discharge data (diagnostic and procedure codes) and hospital characteristics were investigated for years 2009 and 2010. The inclusion criteria were a procedure code for pancreaticoduodenectomy, elective procedure, and a pancreatic or peripancreatic cancer diagnosis. Chi-square test determined statistical significance. A logistic regression model for mortality was created from significant variables. RESULTS: Two-thousand and 958 patients were identified with an average age of 65+/-12 years; 53% were male. The mean length of stay was 15+/-12 days with a mortality of 4% and a complication rate of 57%. Eighty-six percent of pancreaticoduodenectomy occurred in teaching hospitals. Pancreaticoduodenectomy performed in teaching hospitals in the first half of the academic year were associated with higher mortality than in the latter half (5.5% vs. 3.4%, P=0.005). On logistic regression analysis, non-surgical complications are the largest predictor of death (P<0.001) while operations in the latter half of the academic year are associated with decreased mortality (P<0.01). CONCLUSIONS: The timing of pancreaticoduodenectomy for cancer remained more predictive of mortality than age or length of stay; only complications were more predictive of death than time of year. This suggests that there remains a clinically and statistically significant learning curve for trainees in identifying complications; further study is needed to prove that identification of complications leads to a decrease in mortality rate by taking corrective actions.

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[394]

TÍTULO / TITLE: - Ultrasound-aided diagnosis of an insulinoma in a cat.

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

REVISTA / JOURNAL: - Tierarztl Prax Ausg K Kleintiere Heimtiere. 2013;41(5):338-42.

AUTORES / AUTHORS: - Schaub S; Wigger A

INSTITUCIÓN / INSTITUTION: - Sebastian Schaub, Tierarztliche Praxis Dres. Schaub, Waldstrasse 23, 07745 Jena, Germany, Email: sebastian.schaub@vetmed.uni-giessen.de.

RESUMEN / SUMMARY: - A 15-year old, neutered female, domestic shorthaired cat was presented for evaluation of a 3-month history of paroxysmal falling over and trembling. In laboratory work the cat displayed a mild hypoglycemia. Ultrasound revealed a nodule in the left pancreatic lobe and surgical excision was performed. The histological diagnosis was an insulinoma. To the authors knowledge this is the first ultrasound description of an insulinoma in a cat. Up to date the cat has a survival time of 32 months without recurrence of symptoms.

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[395]

TÍTULO / TITLE: - Prognostic impact of hyaluronan and its regulators in pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - PLoS One. 2013 Nov 11;8(11):e80765. doi: 10.1371/journal.pone.0080765.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0080765

AUTORES / AUTHORS: - Cheng XB; Sato N; Kohi S; Yamaguchi K

INSTITUCIÓN / INSTITUTION: - Department of Surgery 1, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan ; Department of Breast Surgery, the Fourth Affiliated Hospital of China Medical University, Shenyang, China.

RESUMEN / SUMMARY: - BACKGROUND: Although pancreatic ductal adenocarcinoma is characterized by an abundant stroma enriched with hyaluronan (HA), the prognostic impact of HA and its regulators remains unknown. METHODS: Using immunohistochemistry, expression patterns of HA and its regulators, including a synthesizing enzyme (HAS2), and a degrading enzyme (HYAL1) were investigated in patients who received surgical resection. The prognostic significance of these markers and other clinicopathological variables was determined using univariate and multivariate analyses. The HA levels were determined quantitatively by enzyme-linked immunosorbent assay (ELISA). RESULTS: We found that strong expressions of HA (P=0.008) and HAS2 (P=0.022) were significantly associated with shorter survival time after surgery. By contrast, weak expression of HYAL1 was significantly associated with poor survival (P=0.001). In multivariate analysis, tumor stage (hazard ratio (HR)=2.76, 95% confidence interval (CI): 1.14-6.66 P=0.024), strong HA expression (HR=6.04, 95%CI: 1.42-25.69 P=0.015), and weak HYAL1 expression (HR=3.16, 95%CI: 1.19-8.40 P=0.021) were independent factors predicting poor survival. ELISA revealed higher concentration of HA in pancreatic cancer tissues than in normal pancreatic tissues (P=0.001). CONCLUSION: These findings suggest, for the first time, that HA and its regulators may have prognostic impact in patients with pancreatic cancer.

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[396]

TÍTULO / TITLE: - Prognostic impact of p16 and p21 on gastroenteropancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - Oncol Lett. 2013 Dec;6(6):1641-1645. Epub 2013 Oct 9.

●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1610

AUTORES / AUTHORS: - Liu S; Chang Y; Ma J; Li X; Li X; Fan J; Huang R; Duan G; Sun X

INSTITUCIÓN / INSTITUTION: - Department of Epidemiology, College of Public Health of Zhengzhou University, Zhengzhou, Henan 450001, P.R. China ; Henan Cancer Research and Control Office, Henan Cancer Hospital, Zhengzhou, Henan 450008, P.R. China.

RESUMEN / SUMMARY: - Aberrant expression of the cell cycle kinase inhibitors, p16 and p21, has been associated with poor prognosis in a number of human malignancies. These proteins may also be involved in the development and progression of gastroenteropancreatic neuroendocrine tumors (GEP-NETs). The present study aimed to investigate protein levels of p16 and p21 in GEP-NETs and to evaluate their clinical significance. p16 and p21 protein expression was tested immunohistochemically in the tissue samples of 68 GEP-NETs. The association between expression and clinicopathological characteristics and overall survival was assessed. Low expression of p16 (no positive nuclear staining) was found in 37 (54%) cases and high p21 expression (>/=5% positive nuclear staining) was detected in 23 (34%) cases. Low p16 protein levels indicated a poorer prognosis for patients graded as G2 subgroup in the univariate analysis (relative risk, 4.4; 95% CI, 1.8-10.6). No significant correlation was found between the expression of p21 and any of the clinicopathological variables. The present study indicates a prognostic relevance for

p16 immunoreactivity. Low levels of p16 protein were associated with a shorter survival in the G2 subgroup of GEP-NETs. p21 protein expression was not identified to be useful as a predictive indicator in GEP-NETs.

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[397]

TÍTULO / TITLE: - Pancreatic cancer: Standing on the shoulders of mice, making an iMPACT on pancreatic cancer.

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

REVISTA / JOURNAL: - Nat Rev Clin Oncol. 2013 Dec;10(12):665. doi: 10.1038/nrclinonc.2013.209. Epub 2013 Nov 5.

●● Enlace al texto completo (gratuito o de pago) 1038/nrclinonc.2013.209

AUTORES / AUTHORS: - Villanueva MT

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[398]

TÍTULO / TITLE: - Squamoid Cyst of Pancreatic Ducts: A Challenging Differential Diagnosis among Benign Pancreatic Cysts.

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):657-60. doi: 10.6092/1590-8577/1905.

AUTORES / AUTHORS: - Milanetto AC; Iaria L; Alaggio R; Pedrazzoli S; Pasquali C

INSTITUCIÓN / INSTITUTION: - Fourth Surgical Clinic, University of Padua. Padua, Italy. ac.milanetto@email.it.

RESUMEN / SUMMARY: - CONTEXT: In the last years, cystic pancreatic lesions are often detected when clinically silent, because of the wider use of diagnostic imaging techniques. First described by Othman in 2007, “squamoid cyst of pancreatic ducts” represents a cystic dilation of ducts, lined by non-keratinized squamous epithelium. We report the first case of squamoid cyst of pancreatic ducts in Italy. CASE REPORT: A 68-year-old woman presented a cystic lesion (4 cm) of the pancreatic tail as incidental finding at MRI. It had a thickened wall, no internal septa and no communication with the Wirsung duct were detected. A CT scan showed a lamellar calcification on its posterior wall. A 18F-FDG-PET was negative. Blood tests were normal, including CEA and CA 19-9. We performed a spleen-preserving distal pancreatectomy. Histology showed a unilocular cyst, with serous fluid and a fibrous wall, with multilayered epithelium without cytological atypias. Immunohistochemistry showed CK 7 positive and CK 5 negative. The patient is still alive and without disease after 42 months of follow-up. CONCLUSIONS: In the English literature only seven cases resected for this cyst type have been reported. No preoperative test can achieve a definitive diagnosis, so surgical resection remains the treatment of choice in order to exclude malignancy. However, after intraoperative frozen section, a limited pancreatic resection can be performed.

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[399]

TÍTULO / TITLE: - Pancreatic paraganglioma: An extremely rare entity and crucial role of immunohistochemistry for diagnosis.

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

REVISTA / JOURNAL: - Indian J Endocrinol Metab. 2013 Sep;17(5):917-9. doi: 10.4103/2230-8210.117217.

●● Enlace al texto completo (gratuito o de pago) 4103/2230-8210.117217

AUTORES / AUTHORS: - Borgohain M; Gogoi G; Das D; Biswas M

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Assam Medical College and Hospital, Dibrugarh, Assam, India.

RESUMEN / SUMMARY: - Paragangliomas are rare neuroendocrine neoplasms arising in extra-adrenal chromaffin cells of autonomic nervous system and histologically akin to chemodectomas. They are rare, affecting about 1 in 2,000,000 population. It is a generic term applied to tumors of paraganglia regardless of the location. In rare instances, paragangliomas present around and involve the pancreas, thereby mimicking any one of the more common primary pancreatic lesions. Pancreatic paraganglioma is an extremely rare tumor. It grows slowly, so radical resection is recommended to achieve curability with good prognosis. These neoplasms present considerable diagnostic difficulty not only for the clinician and radiologist but also for the pathologist. Here, we report a case of a 55-year-old woman who presented with a left-sided abdominal swelling for 3 months duration, initially having clinical suspicion of an ovarian tumor. The radiological imaging revealed a lesion in the tail of pancreas with a differential diagnosis of pancreatic carcinoma and metastatic tumor. Only after exploratory laparotomy, the diagnosis was made as a rare case of pancreatic paraganglioma on the basis of histological examination and immunohistochemistry.

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[400]

TÍTULO / TITLE: - HOXB7 mRNA is overexpressed in pancreatic ductal adenocarcinomas and its knockdown induces cell cycle arrest and apoptosis.

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

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 2;13:451. doi: 10.1186/1471-2407-13-451.

●● Enlace al texto completo (gratuito o de pago) 1186/1471-2407-13-451

AUTORES / AUTHORS: - Chile T; Fortes MA; Correa-Giannella ML; Brentani HP; Maria DA; Puga RD; de Paula Vde J; Kubrusly MS; Novak EM; Bacchella T; Giorgi RR

INSTITUCIÓN / INSTITUTION: - Laboratory for Cellular and Molecular Endocrinology (LIM-25), University of Sao Paulo Medical School, Av, Dr, Arnaldo, 455 # 4305, Sao Paulo, SP, 01246-903, Brazil. rrgiorgi2@hotmail.com.

RESUMEN / SUMMARY: - BACKGROUND: Human homeobox genes encode nuclear proteins that act as transcription factors involved in the control of differentiation and proliferation. Currently, the role of these genes in development and tumor progression has been extensively studied. Recently, increased expression of HOXB7 homeobox gene (HOXB7) in pancreatic ductal adenocarcinomas (PDAC) was shown to correlate with an invasive phenotype, lymph node metastasis and worse survival outcomes, but no influence on cell proliferation or viability was detected. In the present study, the effects arising from the knockdown of HOXB7 in PDAC cell lines was investigated. METHODS: Real time quantitative PCR (qRT-PCR) (Taqman) was employed to assess HOXB7 mRNA expression in 29 PDAC, 6 metastatic tissues, 24 peritumoral tissues and two PDAC cell lines. siRNA was used to knockdown HOXB7 mRNA in the cell lines and its consequences on apoptosis rate and cell proliferation were measured by flow cytometry and MTT assay respectively. RESULTS: Overexpression of HOXB7 mRNA was observed in the tumoral tissues and in the cell lines MIA PaCa-2 and Capan-1. HOXB7 knockdown elicited (1) an increase in the expression of the pro-apoptotic proteins BAX and BAD in both cell lines; (2) a decrease in the expression of the anti-apoptotic protein BCL-2 and in cyclin D1 and an increase in the number of apoptotic cells in the MIA PaCa-2 cell line; (3) accumulation of cell in sub-G1 phase in

both cell lines; (4) the modulation of several biological processes, especially in MIA PaCa-2, such as proteasomal ubiquitin-dependent catabolic process and cell cycle. CONCLUSION: The present study confirms the overexpression of HOXB7 mRNA expression in PDAC and demonstrates that decreasing its protein level by siRNA could significantly increase apoptosis and modulate several biological processes. HOXB7 might be a promising target for future therapies.

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[401]

TÍTULO / TITLE: - Rankings versus reality in pancreatic cancer surgery: a real-world comparison.

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

REVISTA / JOURNAL: - HPB (Oxford). 2013 Nov 7. doi: 10.1111/hpb.12171.

●● Enlace al texto completo (gratuito o de pago) 1111/hpb.12171

AUTORES / AUTHORS: - Chau Z; West JK; Zhou Z; McDade T; Smith JK; Ng SC; Kent TS; Callery MP; Moser AJ; Tseng JF

INSTITUCIÓN / INSTITUTION: - Surgical Outcomes Analysis and Research (SOAR), University of Massachusetts Medical School, Worcester, MA, USA.

RESUMEN / SUMMARY: - BACKGROUND: Patients are increasingly confronted with systems for rating hospitals. However, the correlations between publicized ratings and actual outcomes after pancreatectomy are unknown. METHODS: The Massachusetts Division of Health Care Finance and Policy Hospital Inpatient Discharge Database was queried to identify pancreatic cancer resections carried out during 2005-2009. Hospitals performing fewer than 10 pancreatic resections in the 5-year period were excluded. Primary outcomes included mortality, complications, median length of stay (LoS) and a composite outcomes score (COS) combining primary outcomes. Ranks were determined and compared for: (i) volume, and (ii) ratings identified from consumer-directed hospital ratings including the US News & World Report (USN), Consumer Reports, Healthgrades and Hospital Compare. An inter-rater reliability analysis was performed and correlation coefficients ® between outcomes and ratings, and between rating systems were calculated. RESULTS: Eleven hospitals in which a total of 804 pancreatectomies were conducted were identified. Surgical volume correlated with overall outcome, but was not the strongest indicator. The highest correlation referred to that between USN rank and overall outcome. Mortality was most strongly correlated with Healthgrades ratings (r = 0.50); however, Healthgrades ratings demonstrated poorer correlations with all other outcomes. Consumer Reports ratings showed inverse correlations. CONCLUSIONS: The plethora of publicly available hospital ratings systems demonstrates heterogeneity. Volume remains a good but imperfect indicator of surgical outcomes. Further systematic investigation into which measures predict quality outcomes in pancreatic cancer surgery will benefit both patients and providers.

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[402]

TÍTULO / TITLE: - The use of Multidimensional Data to Identify the Molecular Biomarker for Pancreatic Ductal Adenocarcinoma.

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

REVISTA / JOURNAL: - Biomed Res Int. 2013;2013:798054. doi: 10.1155/2013/798054. Epub 2013 Sep 21.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/798054

AUTORES / AUTHORS: - Zhuang L; Qi Y; Wu Y; Liu N; Fu Y
INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Robotics and System, Bio-X Centre, Harbin Institute of Technology, Harbin, Heilongjiang 150001, China ; Department of Gastroenterology, The Fourth Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang 150001, China.
RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is a lethal disease, and the patient has an extremely poor overall survival with a less than 5% 5-year survival rate. Development of potential biomarkers provides a critical foundation for the diagnosis of PDAC. In this project, we have adopted an integrative approach to simultaneously identify biomarker and generate testable hypothesis from multidimensional omics data. We first examine genes for which expression levels are correlated with survival data. The gene list was screened with TF regulation, predicted miRNA targets information, and KEGG pathways. We identified that 273 candidate genes are correlated with patient survival data. 12 TF regulation gene sets, 11 miRNAs targets gene sets, and 15 KEGG pathways are enriched with these survival genes. Notably, CEBPA/miRNA32/PER2 signaling to the clock rhythm qualifies this pathway as a suitable target for therapeutic intervention in PDAC. PER2 expression was highly associated with survival data, thus representing a novel biomarker for earlier detection of PDAC.

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[403]
TÍTULO / TITLE: - MicroRNA-gene signaling pathways in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Biomed J. 2013 Sep-Oct;36(5):200-8. doi: 10.4103/2319-4170.119690.
●● Enlace al texto completo (gratuito o de pago) 4103/2319-4170.119690
AUTORES / AUTHORS: - Drakaki A; Iliopoulos D
INSTITUCIÓN / INSTITUTION: - Center for Systems Biomedicine, Division of Digestive Diseases, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA.
RESUMEN / SUMMARY: - Pancreatic cancer is the fourth most frequent cause of cancer-related deaths and is characterized by early metastasis and pronounced resistance to chemotherapy and radiation therapy. Despite extensive esearch efforts, there is not any substantial progress regarding the identification of novel drugs against pancreatic cancer. Although the introduction of the chemotherapeutic agent gemcitabine improved clinical response, the prognosis of these patients remained extremely poor with a 5-year survival rate of 3-5%. Thus, the identification of the novel molecular pathways involved in pancreatic oncogenesis and the development of new and potent therapeutic options are highly desirable. Here, we describe how microRNAs control signaling pathways that are frequently deregulated during pancreatic oncogenesis. In addition, we provide evidence that microRNAs could be potentially used as novel pancreatic cancer therapeutics through reversal of chemotherapy and radiotherapy resistance or regulation of essential molecular pathways. Further studies should integrate the deregulated genes and microRNAs into molecular networks in order to identify the central regulators of pancreatic oncogenesis. Targeting these central regulators could lead to the development of novel targeted therapeutic approaches for pancreatic cancer patients.

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[404]
TÍTULO / TITLE: - PAF-Mediated MAPK Signaling Hyperactivation via LAMTOR3 Induces Pancreatic Tumorigenesis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cell Rep. 2013 Oct 22. pii: S2211-1247(13)00549-4. doi: 10.1016/j.celrep.2013.09.026.
●● Enlace al texto completo (gratuito o de pago) 1016/j.celrep.2013.09.026
AUTORES / AUTHORS: - Jun S; Lee S; Kim HC; Ng C; Schneider AM; Ji H; Ying H; Wang H; Depinho RA; Park JI
INSTITUCIÓN / INSTITUTION: - Department of Experimental Radiation Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA.
RESUMEN / SUMMARY: - Deregulation of mitogen-activated protein kinase (MAPK) signaling leads to development of pancreatic cancer. Although Ras-mutation-driven pancreatic tumorigenesis is well understood, the underlying mechanism of Ras-independent MAPK hyperactivation remains elusive. Here, we have identified a distinct function of PCNA-associated factor (PAF) in modulating MAPK signaling. PAF is overexpressed in pancreatic cancer and required for pancreatic cancer cell proliferation. In mouse models, PAF expression induced pancreatic intraepithelial neoplasia with expression of pancreatic cancer stem cell markers. PAF-induced ductal epithelial cell hyperproliferation was accompanied by extracellular signal-regulated kinase (ERK) phosphorylation independently of Ras or Raf mutations. Intriguingly, PAF transcriptionally activated the expression of late endosomal/lysosomal adaptor, MAPK and mTOR activator 3 (LAMTOR3), which hyperphosphorylates MEK and ERK and is necessary for pancreatic cancer cell proliferation. Our results reveal an unsuspected mechanism of mitogenic signaling activation via LAMTOR3 and suggest that PAF-induced MAPK hyperactivation contributes to pancreatic tumorigenesis.

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[405]
TÍTULO / TITLE: - The FAK scaffold inhibitor C4 disrupts FAK-VEGFR-3 signaling and inhibits pancreatic cancer growth.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Oncotarget. 2013 Oct;4(10):1632-46.
AUTORES / AUTHORS: - Kurenova E; Liao J; He DH; Hunt D; Yemma M; Bshara W; Seshadri M; Cance WG
INSTITUCIÓN / INSTITUTION: - Department of Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.
RESUMEN / SUMMARY: - Even with successful surgical resection and perioperative chemotherapy and radiation, pancreatic ductal adenocarcinoma (PDA) has a high incidence of recurrence. Tumor cell survival depends on activation of signaling pathways that suppress the apoptotic stimuli of invasion and metastasis. Focal adhesion kinase (FAK) is a critical signaling molecule that has been implicated in tumor cell survival, invasion and metastasis. We have previously shown that FAK and vascular endothelial growth factor receptor 3 (VEGFR-3) are overexpressed in cancer cells and physically interact to confer a significant survival advantage. We subsequently identified a novel small molecule inhibitor C4 that targeted the VEGFR-3-FAK site of interaction. In this study, we have shown that C4 disrupted the FAK-VEGFR-3 complexes in PDA cells. C4 treatment caused dose-dependent

dephosphorylation and inactivation of the VEGFR-3 and FAK, reduction in cell viability and proliferation, cell cycle arrest and apoptosis in PDA cells. C4 increased the sensitivity of tumor cells to gemcitabine chemotherapy in vitro that lead to apoptosis at nanomolar concentrations of both drugs. C4 reduced tumor growth in vivo in subcutaneous and orthotopic murine models of PDA. The drug alone at low dose, decreased tumor growth; however, concomitant administration with low dose of gemcitabine had significant synergistic effect and led to 70% tumor reduction. Combination of C4 with gemcitabine had a prolonged cytostatic effect on tumor growth after treatment withdrawal. Finally, we report an anecdotal case of stage IV pancreatic cancer treated with gemcitabine in combination with C4 that showed a significant clinical response in primary tumor and complete clinical response in liver metastasis over an eight month period. Taken together, these results demonstrate that targeting the scaffolding function of FAK with a small-molecule FAK-VEGFR-3 inhibitor can be an effective therapeutic strategy against PDA.

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[406]

TÍTULO / TITLE: - Anesthetists approach in a neonate with nesidioblastoma undergoing pancreatectomy.

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

REVISTA / JOURNAL: - J Anaesthesiol Clin Pharmacol. 2013 Jul;29(3):384-6. doi: 10.4103/0970-9185.117108.

●● Enlace al texto completo (gratuito o de pago) 4103/0970-9185.117108

AUTORES / AUTHORS: - Patel K; Shikare M; Chavan D; Sawant P

INSTITUCIÓN / INSTITUTION: - Department of Pediatric Anesthesiology, B. J. Wadia Hospital, Parel, Mumbai, India.

RESUMEN / SUMMARY: - Persistent hyperinsulinemic hypoglycemia of infancy (PHHI) is rare, but an important cause of hypoglycemia in infants, associated with a number of structural abnormalities of the endocrine pancreas is collectively termed as “Islet cell dysmaturation syndrome.” We present the anesthetic management in a clinically diagnosed case of PHHI in a 22 days old full term child, undergoing Subtotal Pancreatectomy. We have discussed the challenges faced in the intra-operative period in managing this neonate for pancreatic resection surgery with focus on intra-operative management of blood glucose levels.

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[407]

TÍTULO / TITLE: - Chromosome instability and carcinogenesis: Insights from murine models of human pancreatic cancer associated with BRCA2 inactivation.

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

REVISTA / JOURNAL: - Mol Oncol. 2013 Nov 6. pii: S1574-7891(13)00145-2. doi: 10.1016/j.molonc.2013.10.005.

●● Enlace al texto completo (gratuito o de pago) 1016/j.molonc.2013.10.005

AUTORES / AUTHORS: - Cassidy LD; Liau SS; Venkitaraman AR

INSTITUCIÓN / INSTITUTION: - University of Cambridge, Medical Research Council Cancer Cell Unit, Hutchison/MRC Research Centre, Hills Road, Cambridge CB2 0XZ, United Kingdom.

RESUMEN / SUMMARY: - Chromosomal instability is a hallmark of human cancer cells, but its role in carcinogenesis remains poorly resolved. Insights into this role have emerged from studies on the tumour suppressor BRCA2, whose inactivation in human

cancers causes chromosomal instability through the loss of essential functions of the BRCA2 protein in the normal mechanisms responsible for the replication, repair and segregation of DNA during cell division. Humans who carry heterozygous germline mutations in the BRCA2 gene are highly predisposed to cancers of the breast, ovary, pancreas, prostate and other tissues. Here, we review recent studies that describe genetically engineered mouse models (GEMMs) for pancreatic cancer associated with BRCA2 mutations. These studies not only surprisingly show that BRCA2 does not follow the classical Knudson “two hit” paradigm for tumour suppression, but also highlight features of the interplay between TP53 inactivation and carcinogenesis in the context of BRCA2 deficiency. Thus, the models reveal novel aspects of cancer evolution in carriers of germline BRCA2 mutations, provide new insights into the tumour suppressive role of BRCA2, and establish valuable new preclinical settings for testing approaches to pancreatic cancer therapy; together, these features emphasize the value of GEMMs in cancer research.

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[408]

TÍTULO / TITLE: - Role of radiotherapy for pancreatobiliary neuroendocrine tumors.

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

REVISTA / JOURNAL: - Radiat Oncol J. 2013 Sep;31(3):125-30. doi: 10.3857/roj.2013.31.3.125. Epub 2013 Sep 30.

●● Enlace al texto completo (gratuito o de pago) 3857/roj.2013.31.3.125

AUTORES / AUTHORS: - Lee J; Choi J; Choi C; Seong J

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - PURPOSE: We investigated the role of radiotherapy (RT) for pancreatobiliary neuroendocrine tumors (PB-NETs). MATERIALS AND METHODS: We identified 9 patients with PB-NETs who received RT between January 2005 and March 2012. Of these 9 patients, 4 were diagnosed with NETs in the pancreas and 5 were diagnosed with NETs in the gallbladder. All patients received RT to the primary tumor or resection bed with a median total irradiation dose of 50.4 Gy, with or without chemotherapy. RESULTS: The tumor response rate and tumor control rate in the RT field were 60% and 100 %, respectively. All 4 patients who underwent surgery had no evidence of disease in the RT field. Of the 5 patients who received RT to the primary gross tumor, 1 had complete response, 2 had partial response, and 2 had stable disease in the RT field. The median time to progression was 11 months. Of the 9 patients, four patients had no progression, and 5 patients had progression of disease (locoregional, 2; distant, 2; locoregional/distant, 1). Of the 4 patients without progression, 3 were treated with RT in adjuvant or neoadjuvant setting, and one received RT to primary tumor. One patient experienced radiation-induced duodenitis at 3 months after concurrent chemoradiation without treatment-related mortality. CONCLUSION: RT can yield local control for advanced PB-NETs. RT should be considered an essential part of multimodality treatment in management of advanced PB-NETs.

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[409]

TÍTULO / TITLE: - Differentiation of mucinous cystic neoplasm and cystic changes associated with pancreatic adenocarcinoma.

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

●● Cita: British Medical J. (BMJ): <> Case Rep. 2013 Nov 5;2013. pii: bcr2013201208. doi: 10.1136/bcr-2013-201208.

●● Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-201208

AUTORES / AUTHORS: - Ha TH; Jeon TJ; Park JY

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology Department of Internal Medicine, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Republic of Korea.

RESUMEN / SUMMARY: - A 63-year-old woman presented to the hospital with persistent nausea, dyspepsia and weight loss for 6 months. Abdomen CT showed a low-attenuation mass, approximately 7.6 cm diameter, in the region of the body and tail of the pancreas. Cystic lesions, 5.5x4.9 cm and 4.6x3.7 cm in size, were observed in the body and tail of the pancreas, respectively, associated with the low-attenuation mass. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) revealed fetal carcinoembryonic antigen levels of >1000 ng/mL and necrotic cells with no malignant cells. On the basis of the imaging and EUS-FNA results, a putative diagnosis of mucinous cystadenoma accompanying pancreatic adenocarcinoma was made, and distal pancreatectomy and splenectomy were performed. Final biopsy using the surgical specimen confirmed pancreatic adenocarcinoma with moderate differentiation accompanied by degenerative cystic changes.

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[410]

TÍTULO / TITLE: - En masse resection of pancreas, spleen, celiac axis, stomach, kidney, adrenal, and colon for invasive pancreatic corpus and tail tumor.

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

REVISTA / JOURNAL: - Case Rep Surg. 2013;2013:376035. doi: 10.1155/2013/376035. Epub 2013 Sep 15.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/376035

AUTORES / AUTHORS: - Kutluturk K; Alam AH; Kayaalp C; Otan E; Aydin C

INSTITUCIÓN / INSTITUTION: - Inonu University, Malatya, Turkey.

RESUMEN / SUMMARY: - Providing a more comfortable life and a longer survival for pancreatic corpus/tail tumors without metastasis depends on the complete resection. Recently, distal pancreatectomy with celiac axis resection was reported as a feasible and favorable method in selected pancreatic corpus/tail tumors which had invaded the celiac axis. Additional organ resections to the celiac axis were rarely required, and when necessary it was included only a single extra organ resection such as adrenal or intestine. Here, we described a distal pancreatic tumor invading most of the neighboring organs-stomach, celiac axis, left renal vein, left adrenal gland, and splenic flexure were treated by en bloc resection of all these organs. The patient was a 60-year-old man without any severe medical comorbidities. Postoperative course of the patient was uneventful, and he was discharged on postoperative day eight without any complication. Histopathology and stage of the tumor were adenocarcinoma and T4 N1 M0, respectively. Preoperative back pain of the patient was completely relieved in the postoperative period. As a result, celiac axis resection for pancreatic cancer is an extensive surgery, and a combined en masse resection of the invaded neighboring organs is a more extensive surgery than the celiac axis resection alone. This more extensive surgery is safe and feasible for selected patients with pancreatic cancer.

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[411]

TÍTULO / TITLE: - Radiologic Resectability Assessment in Pancreatic Cancer.

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

REVISTA / JOURNAL: - Rofo. 2013 Sep 30.

●● Enlace al texto completo (gratuito o de pago) 1055/s-0033-1350190

AUTORES / AUTHORS: - Denecke T; Grieser C; Neuhaus P; Bahra M

INSTITUCIÓN / INSTITUTION: - Institute of Radiology, Campus Virchow-Klinikum, Charite - Universitatsmedizin Berlin.

RESUMEN / SUMMARY: - Complete tumor resection is still the only potentially curative therapy option for patients with ductal adenocarcinoma of the pancreas. Surgical exploration is the gold standard for the determination of tumor resectability. Radiological resectability assessment is of great importance because many clearly unresectable cases can be identified preoperatively and it became essential for surgical planning. The evolving surgical and radiological techniques demand a continuous reappraisal of radiological criteria in resectability assessment. In the following, the criteria for resection planning are described along with surgical management and the role of radiology in some innovative surgical concepts is explained.Citation Format:

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[412]

TÍTULO / TITLE: - Metachronous pancreatic head ductal carcinoma three years after resection of gallbladder cancer.

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

REVISTA / JOURNAL: - Int J Clin Exp Med. 2013 Sep 25;6(9):828-31.

AUTORES / AUTHORS: - Chen D; Yan J; Mou Y

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University Hangzhou 310016, Zhejiang Province, China.

RESUMEN / SUMMARY: - We report a rare case of female patient with metachronous gallbladder cancer and pancreatic head ductal carcinoma. At the age of 53 years, the patient underwent a cholecystectomy and resection of the liver bed for gallbladder cancer. The post-operation diagnosis was a well-differentiated adenocarcinoma with serosa involvement(T3N0M0, stage IIA). Three years later, an irregular and enhanced 2.4 cm mass in the pancreatic head with obviously pancreatic duct dilated was found by abdominal imaging. We considered it as pancreatic head cancer and performed pancreaticoduodenectomy. The histological diagnosis was a pancreatic ductal carcinoma (T2N0M0, stage I). No recurrence was found after thirty-three months follow up.

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[413]

TÍTULO / TITLE: - A Review of the Current Status and Concept of the Emerging Implications of Zinc and Zinc Transporters in the Development of Pancreatic Cancer.

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

REVISTA / JOURNAL: - Pancreat Disord Ther. 2013;Suppl 4. pii: 002.

●● Enlace al texto completo (gratuito o de pago) 4172/2165-7092.S4-002

AUTORES / AUTHORS: - Costello LC; Franklin RB

INSTITUCIÓN / INSTITUTION: - Department of Oncology and Diagnostic Sciences, University of Maryland Dental School and The University of Maryland Greenebaum Cancer Center, Baltimore, Maryland, USA.

RESUMEN / SUMMARY: - Pancreatic cancer (adenocarcinoma) remains a deadly untreatable cancer with no effective early detection procedure. Little is known concerning the factors involved in the development of pancreatic malignancy, which impedes advancements in its treatment and detection. Altered cellular zinc has been implicated in several cancers. Recent studies provide evidence that zinc and zinc transporters are important factors in pancreatic cancer. This review discusses the current information relating to the status of zinc and zinc transporters in human pancreatic adenocarcinoma. Relationships of the physiology and biochemistry of zinc in mammalian cells are presented, which should be applied to the conduct, interpretation, and translational application of human studies and experimental models. Evidence from human pancreatic tissue studies supports a new concept of the role of zinc in the development of pancreatic adenocarcinoma. The zinc level of the normal ductal and acinar epithelium is markedly decreased in the development of the malignant cells and the premalignant PanIN cells. ZIP3 is identified as the likely zinc uptake transporter, which is down regulated concurrently with the loss of zinc. Ras responsive binding protein (RREB1) is identified as the possible transcription factor involved in the silencing of ZIP3 expression. The evidence supports the current views of transdifferentiation of PanIN epithelium to ductal adenocarcinoma, and the possibility that acinar epithelial dedifferentiation might be a source of premalignant cells. These zinc-associated events occur early in oncogenesis to protect the malignant cells from the cytotoxic effects of zinc levels that exist in the normal cells. Hopefully, this presentation will stimulate interest in and support for much needed research into the implications of zinc and zinc transporters as important events in pancreatic carcinogenesis. The potential exists for the RREB1-ZIP3-zinc concept and/or other implications of zinc as new approaches for the development of effective treatment and for diagnostic biomarkers for pancreatic cancer.

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[414]

TÍTULO / TITLE: - Tumor necrosis factor induces tumor promoting and anti-tumoral effects on pancreatic cancer via TNFR1.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 30;8(9):e75737. doi: 10.1371/journal.pone.0075737.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0075737

AUTORES / AUTHORS: - Chopra M; Lang I; Salzmann S; Pachel C; Kraus S; Bauerlein CA; Brede C; Garrote AL; Mattenheimer K; Ritz M; Schwinn S; Graf C; Schafer V; Frantz S; Einsele H; Wajant H; Beilhack A

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine II, Wurzburg University Clinics, Wurzburg, Germany ; Center for Interdisciplinary Clinical Research, Wurzburg University, Wurzburg, Germany.

RESUMEN / SUMMARY: - Multiple activities are ascribed to the cytokine tumor necrosis factor (TNF) in health and disease. In particular, TNF was shown to affect carcinogenesis in multiple ways. This cytokine acts via the activation of two cell surface receptors, TNFR1, which is associated with inflammation, and TNFR2, which was shown to cause anti-inflammatory signaling. We assessed the effects of TNF and its

two receptors on the progression of pancreatic cancer by in vivo bioluminescence imaging in a syngeneic orthotopic tumor mouse model with Panc02 cells. Mice deficient for TNFR1 were unable to spontaneously reject Panc02 tumors and furthermore displayed enhanced tumor progression. In contrast, a fraction of wild type (37.5%), TNF deficient (12.5%), and TNFR2 deficient mice (22.2%) were able to fully reject the tumor within two weeks. Pancreatic tumors in TNFR1 deficient mice displayed increased vascular density, enhanced infiltration of CD4(+) T cells and CD4(+) forkhead box P3 (FoxP3)(+) regulatory T cells (Treg) but reduced numbers of CD8(+) T cells. These alterations were further accompanied by transcriptional upregulation of IL4. Thus, TNF and TNFR1 are required in pancreatic ductal carcinoma to ensure optimal CD8(+) T cell-mediated immunosurveillance and tumor rejection. Exogenous systemic administration of human TNF, however, which only interacts with murine TNFR1, accelerated tumor progression. This suggests that TNFR1 has basically the capability in the Panc02 model to trigger pro-and anti-tumoral effects but the spatiotemporal availability of TNF seems to determine finally the overall outcome.

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[415]

TÍTULO / TITLE: - Role of endoscopic ultrasonography in pancreatic cystic neoplasms: Where do we stand and where will we go?

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

REVISTA / JOURNAL: - Dig Endosc. 2013 Nov 13. doi: 10.1111/den.12202.

●● Enlace al texto completo (gratuito o de pago) 1111/den.12202

AUTORES / AUTHORS: - Nakai Y; Isayama H; Itoi T; Yamamoto N; Kogure H; Sasaki T; Hirano K; Tada M; Koike K

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan.

RESUMEN / SUMMARY: - We increasingly encounter pancreatic cystic neoplasms (PCN) in clinical practice and the differential diagnoses vary widely from benign to malignant. There is no 'one and only' diagnostic procedure for PCN. Multiple modalities including computed tomography, magnetic resonance imaging, endoscopic retrograde cholangiopancreatography and endoscopic ultrasound (EUS) are widely used, but EUS has the advantage of anatomical proximity to the pancreas and upper gastrointestinal tract. In addition, EUS-guided fine-needle aspiration (EUS-FNA) provides both cytological evaluation and cyst fluid analysis. Although the role of EUS-FNA for PCN is established, the sensitivity of cytology is low and cyst fluid analysis is only useful for differentiation between mucinous and non-mucinous cysts. Recently, novel through-the-needle imaging under EUS-FNA, such as confocal laserendomicroscopy, is expected to attribute to a better diagnostic yield. Moreover, feasibility of cyst ablation has been reported and the role of EUS has expanded from diagnosis to treatment. However, clinical impact of cyst ablation in terms of safety, efficacy and cost-effectiveness should be validated further. In summary, EUS and EUS-guided intervention does and will play a central role in the management of PCN from surveillance to treatment, but many clinical questions remain unanswered, which warrants well-designed prospective clinical trials.

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[416]

TÍTULO / TITLE: - Targeting and Cytotoxicity of SapC-DOPS Nanovesicles in Pancreatic Cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Oct 4;8(10):e75507. doi: 10.1371/journal.pone.0075507.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0075507
AUTORES / AUTHORS: - Chu Z; Abu-Baker S; Palascak MB; Ahmad SA; Franco RS; Qi X
INSTITUCIÓN / INSTITUTION: - Division of Hematology/Oncology, Department of Internal Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio, United States of America.
RESUMEN / SUMMARY: - Only a small number of promising drugs target pancreatic cancer, which is the fourth leading cause of cancer deaths with a 5-year survival of less than 5%. Our goal is to develop a new biotherapeutic agent in which a lysosomal protein (saposin C, SapC) and a phospholipid (dioleoylphosphatidylserine, DOPS) are assembled into nanovesicles (SapC-DOPS) for treating pancreatic cancer. A distinguishing feature of SapC-DOPS nanovesicles is their high affinity for phosphatidylserine (PS) rich microdomains, which are abnormally exposed on the membrane surface of human pancreatic tumor cells. To evaluate the role of external cell PS, in vitro assays were used to correlate PS exposure and the cytotoxic effect of SapC-DOPS in human tumor and nontumorigenic pancreatic cells. Next, pancreatic tumor xenografts (orthotopic and subcutaneous models) were used for tumor targeting and therapeutic efficacy studies with systemic SapC-DOPS treatment. We observed that the nanovesicles selectively killed human pancreatic cancer cells in vitro by inducing apoptotic death, whereas untransformed cells remained unaffected. This in vitro cytotoxic effect correlated to the surface exposure level of PS on the tumor cells. Using xenografts, animals treated with SapC-DOPS showed clear survival benefits and their tumors shrank or disappeared. Furthermore, using a double-tracking method in live mice, we showed that the nanovesicles were specifically targeted to orthotopically-implanted, bioluminescent pancreatic tumors. These data suggest that the acidic phospholipid PS is a biomarker for pancreatic cancer that can be effectively targeted for therapy utilizing cancer-selective SapC-DOPS nanovesicles. This study provides convincing evidence in support of developing a new therapeutic approach to pancreatic cancer.

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[417]
TÍTULO / TITLE: - Peroral pancreatoscopy using the SpyGlass system for the assessment of intraductal papillary mucinous neoplasm of the pancreas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Hepatobiliary Pancreat Sci. 2013 Oct 14. doi: 10.1002/jhbp.44.
●● Enlace al texto completo (gratuito o de pago) 1002/jhbp.44
AUTORES / AUTHORS: - Nagayoshi Y; Aso T; Ohtsuka T; Kono H; Ideno N; Igarashi H; Takahata S; Oda Y; Ito T; Tanaka M
INSTITUCIÓN / INSTITUTION: - Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan.
RESUMEN / SUMMARY: - BACKGROUND: Peroral pancreatoscopy (POPS) using a mother-baby endoscope system is often useful for assessment of intraductal papillary mucinous neoplasm (IPMN) of the pancreas with main pancreatic duct (MPD)

involvement, but is not widely used for several reasons. The aim of this study was to evaluate the usefulness of the SpyGlass Direct Visualization System for assessment of IPMN. METHODS: Seventeen patients diagnosed with possible IPMN with MPD dilation underwent peroral pancreatoscopy using the SpyGlass system at our institution. The quality of visualization and the sensitivities of cytological and pathological investigations for diagnosing malignant lesions were evaluated. RESULTS: Peroral pancreatoscopy was performed using the SpyScope in 12 patients and an endoscopic retrograde cholangiopancreatography (ERCP) catheter in five patients. Sufficient visualization was achieved in 92% of cases using the SpyScope and 40% of cases using the ERCP catheter. Biopsy under direct visualization was successful in seven patients. Biopsy specimens showed adenocarcinoma in one patient, benign neoplastic epithelium in five patients, and regenerative changes in one patient; and had 25% sensitivity and 100% specificity for detecting malignancy. SpyGlass pancreatoscopy with irrigation cytology had 100% sensitivity and 100% specificity for detecting malignancy. SpyGlass pancreatoscopy was useful for determining the operative excision line in three patients. There were no severe procedure-related adverse events. CONCLUSIONS: Peroral pancreatoscopy using the SpyGlass system seems to be feasible and useful for assessment of IPMN with a dilated MPD.

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[418]

TÍTULO / TITLE: - Secondary varicocele caused by pancreatic pseudocyst obstructing testicular venous drainage.

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):674-5. doi: 10.6092/1590-8577/1974.

AUTORES / AUTHORS: - Aswani Y; Hira P

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Seth GS Medical College and KEM Hospital. Mumbai, India. yashant_aswani@rediffmail.com.

RESUMEN / SUMMARY: - A pseudocyst is a fluid/debris collection that occurs as a complication of pancreatitis. It can be symptomatic and cause compression of the surrounding structures. Our case report highlights a 29-year-old male who presented with secondary varicocele on left side caused by a huge pseudocyst seen to compress the left renal and testicular veins.

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[419]

TÍTULO / TITLE: - Deleted in liver cancer-1 inhibits cell growth and tumorigenicity in human pancreatic cancer.

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

REVISTA / JOURNAL: - Oncol Lett. 2013 Aug;6(2):521-524. Epub 2013 Jun 18.

●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1415

AUTORES / AUTHORS: - Zheng Z; Tan C; Xiang G; Mai G; Liu X

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, The Third People's Hospital of Chengdu, The Second Affiliated Hospital of Chengdu, Chongqing Medical University, Chengdu, Sichuan 610031, P.R. China.

RESUMEN / SUMMARY: - Deleted in liver cancer-1 (DLC-1) has been isolated from primary hepatocellular carcinoma and demonstrated to be a potential tumor suppressor gene. The aim of the present study was to observe the effect of the DLC-1 gene on pancreatic cancer cell growth and evaluate the feasibility of using the DLC-1 gene in

gene therapy for pancreatic cancer. A recombinant plasmid (pcDNA3.1/DLC-1) was transfected into PANC-1 cells by liposomes and then the pre-established human PANC-1 pancreatic carcinoma cells were injected into athymic nude mice via the tail vein. The results showed that the overexpression of DLC-1 in the PANC-1 cells inhibited cell proliferation in vitro, while the act of introducing DLC-1 reduced tumorigenicity in the nude mice. The findings suggest that DLC-1 may have an effect on the pathogenesis of pancreatic cancer. The DLC-1 gene may be a promising target in gene therapy for pancreatic cancer.

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[420]

TÍTULO / TITLE: - Uncommon lymphoepithelial cyst with sebaceous glands of the pancreas.

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

REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):632-5. doi: 10.6092/1590-8577/1670.

AUTORES / AUTHORS: - Nakamura T; Osaka Y; Ishikawa S; Sako H; Akamatsu N; Yamamoto Y; Hosokawa Y; Yoshimura N

INSTITUCIÓN / INSTITUTION: - Department of Organ Transplantation and General Surgery, Kyoto Prefectural University of Medicine. Kamigyo-ku, Kyoto, Japan. tsukasa@koto.kpu-m.ac.jp.

RESUMEN / SUMMARY: - CONTEXT: Lymphoepithelial cysts with sebaceous glands of the pancreas are extremely rare, with only 7 cases, including this case, published in English literature. CASE REPORT: We herein present the case of a 67-year-old Asian man who underwent a resection of a lymphoepithelial cyst of the pancreas during the follow up care for lung cancer. Fourteen years previously he underwent a right lower lobectomy at the right segment nine for lung cancer. A 20 mm mass in the body of the pancreas was identified by CT scan 4 years ago, and the diagnosis was intraductal papillary mucinous neoplasm (IPMN) at that time. Over a 5-year period, this mass grew to 42 mm without dilatation of the main pancreatic duct. The preoperative evaluation, including endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA), indicated a cystic neoplasm with suspicion of malignancy. Intraoperative frozen section revealed a squamous-lined cyst accompanied by sebaceous glands without any malignant findings. Following this pathological finding, resection of the cyst was performed. Consequently, microscopic examination revealed that it was a lymphoepithelial cyst with sebaceous glands of the pancreas. CONCLUSIONS: Pancreatic lymphoepithelial cysts can be cured by conservative resection, but if they are asymptomatic and are diagnosed before surgery, no treatment is necessary. To our knowledge, this is the first ever published case of a lymphoepithelial cyst with sebaceous glands of the pancreas, which was found during the follow up care for lung cancer.

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[421]

TÍTULO / TITLE: - Synergistic Effects of Concurrent Blockade of PI3K and MEK Pathways in Pancreatic Cancer Preclinical Models.

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

REVISTA / JOURNAL: - PLoS One. 2013 Oct 9;8(10):e77243. doi: 10.1371/journal.pone.0077243.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0077243

AUTORES / AUTHORS: - Zhong H; Sanchez C; Spitrzer D; Plambeck-Suess S; Gibbs J; Hawkins WG; Denardo D; Gao F; Pufahl RA; Lockhart AC; Xu M; Linehan D; Weber J; Wang-Gillam A

INSTITUCIÓN / INSTITUTION: - Division of Oncology, Department of Medicine, Washington University in St. Louis, St. Louis, Missouri, United States of America.

RESUMEN / SUMMARY: - Patients with pancreatic cancer have dismal prognoses, and novel therapies are urgently needed. Mutations of the KRAS oncogene occur frequently in pancreatic cancer and represent an attractive target. Direct targeting of the predominant KRAS pathways have been challenging and research into therapeutic strategies have been now refocused on pathways downstream of KRAS, phosphoinositide 3-kinase (PI3K) and mitogen-activated protein kinase (MAPK [MEK]). We hypothesized that concurrent inhibition of the PI3K and MEK pathways would result in synergistic antitumor activity, as it would circumvent the compensatory feedback loop between the two pathways. We investigated the combined effect of the PI3K inhibitor, GDC0941, and the MEK inhibitor, AZD6244, on cell viability, apoptosis and cell signaling in a panel of pancreatic cancer cell lines. An in vivo analysis was conducted on pancreatic cancer xenografts. While BxPC-3 (KRAS wild type) and MIA PaCa-2 (KRAS mutated) cell lines were sensitive to GDC0941 and AZD6244 as single agents, synergistic inhibition of tumor cell growth and induction of apoptosis were observed in both cell lines when the two drugs were combined. Interestingly, phosphorylation of the cap-dependent translational components, 4E-binding protein (p-4E-BP1) and S6 was found to be closely associated with sensitivity to GDC0941 and AZD6244. In BxPC-3 cell xenografts, survival differences were observed between the control and the AZD6244, GDC0941, and combination groups. Our study provides the rationale for concurrent targeting of the PI3K and MEK pathways, regardless of KRAS status, and suggests that phosphorylation of 4E-BP1and S6 can serve as a predictive biomarker for response to treatment.

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[422]

TÍTULO / TITLE: - Gastric somatostatinoma: an extremely rare cause of upper gastrointestinal bleeding.

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

REVISTA / JOURNAL: - Clin Endosc. 2013 Sep;46(5):582-5. doi: 10.5946/ce.2013.46.5.582. Epub 2013 Sep 30.

●● Enlace al texto completo (gratuito o de pago) 5946/ce.2013.46.5.582

AUTORES / AUTHORS: - Prachayakul V; Aswakul P; Deesomsak M; Pongpaibul A

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology, Department of Internal Medicine, Siriraj Hospital, Mahidol University Faculty of Medicine, Bangkok, Thailand.

RESUMEN / SUMMARY: - A 49-year-old woman presented with chronic abdominal discomfort, significant weight loss, and chronic intermittent diarrhea. She suddenly developed massive upper gastrointestinal bleeding and was referred for further treatment. Endoscopy indicated a large mass in the upper gastric body with antral and duodenal bulb involvement. Endosonography showed a large well-defined isoechoic gastric subepithelial mass with multiple intra-abdominal and peripancreatic lymphadenopathy, suspected to be malignant on the basis of fine needle aspiration cytology. The tumor was surgically removed, and histopathology showed typical characteristics of a neuroendocrine tumor. On the basis of immunohistochemical staining, somatostatinoma, a rare neuroendocrine tumor, was diagnosed.

Gastrointestinal bleeding is a rare presentation and the stomach is an uncommon tumor location.

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[423]

TÍTULO / TITLE: - Minimally invasive management of pancreatic pseudocysts.

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

REVISTA / JOURNAL: - Wideochir Inne Tech Malo Inwazyjne. 2013 Sep;8(3):211-5. doi: 10.5114/wiitm.2011.33809. Epub 2013 May 27.

●● Enlace al texto completo (gratuito o de pago) 5114/wiitm.2011.33809

AUTORES / AUTHORS: - Sileikis A; Beisa A; Zdanyte E; Jurevicius S; Strupas K

INSTITUCIÓN / INSTITUTION: - Clinic of Gastroenterology, Nephrology and Surgery, Medical Faculty, Vilnius University, Lithuania.

RESUMEN / SUMMARY: - INTRODUCTION: The laparoscopic and endoscopic approaches to internal drainage of pancreatic pseudocysts (PP) are the current minimally invasive management options. Indications, and early and late results of endoscopic and laparoscopic approaches are being discussed. AIM: To present experience in treatment of PP by laparoscopic pseudocystogastrostomy (LPGS) and endoscopic pseudocystogastrostomy (EPGS) and to compare results, feasibility and safety. MATERIAL AND METHODS: THIRTY PATIENTS UNDERWENT SURGICAL INTERVENTION: 18 patients - LPGS (group I), 12 - EPGS (group II). Groups were compared by age, gender, pancreatic pseudocysts's age, diameter and localization, as well as intraoperative, early and late postoperative complications. RESULTS: GENDER DISTRIBUTION, GROUP I: 14 (77.8%) men and 4 (22.2%) women, group II: 4 (33.3%) men and 8 (66.7%) women, p = 0.02. Average cyst diameter: group I - 149.9 +/-52.1 mm, group II - 119 +/-37.9 mm, p = 0.07. Average time between diagnosis and operation performance: group I - 12 (3-60) months, group II - 8 (2-36) months, p = 0.19. Neither in group I nor in group II did intraoperative complications occur. Early postoperative complications were divided into minor and major. Early minor complications: group I - 2 (11.1%), group II - 0, p = 0.5. Early major complications: group I - 0, group II - 2 (16.7%), p = 0.15. Late postoperative complications: group I - 0, group II - 1 (8.3%), p = 0.4. In group I there was no case, whereas in II group there was 1 (8.3%) case of recidivation, p = 0.4. CONCLUSIONS: For selected patients both minimally invasive methods are equally safe an effective. For comprehensive evaluation of methods prospective trials are needed.

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[424]

TÍTULO / TITLE: - Carcinogenesis of pancreatic adenocarcinoma: precursor lesions.

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

REVISTA / JOURNAL: - Int J Mol Sci. 2013 Sep 30;14(10):19731-62. doi: 10.3390/ijms141019731.

●● Enlace al texto completo (gratuito o de pago) 3390/ijms141019731

AUTORES / AUTHORS: - Gnoni A; Licchetta A; Scarpa A; Azzariti A; Brunetti AE; Simone G; Nardulli P; Santini D; Aieta M; Delcuratolo S; Silvestris N

INSTITUCIÓN / INSTITUTION: - Medical Oncology Unit, Hospital Vito Fazzi, Lecce 73100, Italy. n.silvestris@oncologico.bari.it.

RESUMEN / SUMMARY: - Pancreatic adenocarcinoma displays a variety of molecular changes that evolve exponentially with time and lead cancer cells not only to survive, but also to invade the surrounding tissues and metastasise to distant sites. These

changes include: genetic alterations in oncogenes and cancer suppressor genes; changes in the cell cycle and pathways leading to apoptosis; and also changes in epithelial to mesenchymal transition. The most common alterations involve the epidermal growth factor receptor (EGFR) gene, the HER2 gene, and the K-ras gene. In particular, the loss of function of tumor-suppressor genes has been documented in this tumor, especially in CDKN2a, p53, DPC4 and BRCA2 genes. However, other molecular events involved in pancreatic adenocarcinoma pathogenesis contribute to its development and maintenance, specifically epigenetic events. In fact, key tumor suppressors that are well established to play a role in pancreatic adenocarcinoma may be altered through hypermethylation, and oncogenes can be upregulated secondary to permissive histone modifications. Indeed, factors involved in tumor invasiveness can be aberrantly expressed through dysregulated microRNAs. This review summarizes current knowledge of pancreatic carcinogenesis from its initiation within a normal cell until the time that it has disseminated to distant organs. In this scenario, highlighting these molecular alterations could provide new clinical tools for early diagnosis and new effective therapies for this malignancy.

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[425]

TÍTULO / TITLE: - CD 99 immunocytochemistry in solid pseudopapillary tumor of pancreas: A study on fine-needle aspiration cytology smears.

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

REVISTA / JOURNAL: - J Cytol. 2013 Jul;30(3):151-5. doi: 10.4103/0970-9371.117645.

●● Enlace al texto completo (gratuito o de pago) 4103/0970-9371.117645

AUTORES / AUTHORS: - Ghosh R; Mallik SR; Mathur SR; Iyer VK

INSTITUCIÓN / INSTITUTION: - Department of Pathology, All India Institute of Medical Sciences, New Delhi, India.

RESUMEN / SUMMARY: - BACKGROUND: Solid pseudopapillary tumor of pancreas (SPTP) is a rare pancreatic tumor of uncertain histogenesis usually affecting young women. Though these tumors have characteristic cytomorphology, it is sometimes difficult to differentiate them from neuroendocrine tumors of the pancreas. We reviewed cases of SPTP to delineate the diagnostic cytological features and also observed utility of CD 99 (MIC 2) immunostaining to aid in the diagnosis of this tumor. AIMS: This study was designed to demonstrate the utility of CD 99 immunostaining along with cytological features for making a pre-operative diagnosis and delineating it from the neuroendocrine tumor of pancreas which is a close mimic. MATERIALS AND METHODS: Cytomorphological features of 11 cases of solid pseudopapillary neoplasm diagnosed by pre-operative fine-needle aspiration cytology (FNAC) at our institute were reviewed. Immunocytochemistry for CD 99 was also performed on the smears. RESULTS: All the cases had cellular smears with monomorphic cells lying singly, as loosely cohesive clusters as well as forming delicate pseudopapillae. Presence of intra and extra-cellular basement membrane material, background foamy macrophages and nuclear grooves were the other salient features. Immunocytochemistry for CD 99 could be performed on eight cases and demonstrated typical paranuclear dot-like positivity. CONCLUSIONS: Pre-operative early diagnosis of SPTP can be made by FNAC which can further be aided by CD 99 immunocytochemistry.

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[426]

TÍTULO / TITLE: - Mucinous cystic neoplasm in heterotopic pancreas presenting as colonic polyp.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Nov 10;14(6):671-3. doi: 10.6092/1590-8577/1943.
AUTORES / AUTHORS: - Abraham J; Agrawal V; Behari A
INSTITUCIÓN / INSTITUTION: - Department of Surgical Gastroenterology, Sanjay Gandhi Post-Graduate Institute of Medical Sciences. Lucknow, India. joyabrahamdr@gmail.com.
RESUMEN / SUMMARY: - CONTEXT: Pancreatic heterotopia in itself is rare in the colon and to the best of our knowledge a neoplasm arising in a heterotopic tissue in the colon has not been reported. We herein report a pancreatic cystic neoplasm arising from heterotopic pancreatic tissue in colon. CASE REPORT: A 44-year-old lady presented with a history of lower abdominal colic, associated with mucoid loose stools 10-15 times/day. Fecal occult blood was positive on two occasions. On examination, a vague mass was palpable in the left upper quadrant of abdomen. Colonoscopy showed a polypoid growth at the splenic flexure of colon, which on biopsy was reported to be an inflammatory polyp. She underwent a laparoscopic converted to open left hemicolectomy. Post-operatively she developed a intra-abdominal collection which formed a controlled pancreatic fistula after percutaneous drainage. Histopathology revealed pancreatic heterotopia with pancreatic mucinous cystic neoplasm. CONCLUSION: Despite advances in patient care, preoperative diagnosis of heterotopic pancreas is difficult.

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[427]
TÍTULO / TITLE: - Cystic fibrosis of pancreas and nephrotic syndrome: a rare association.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Korean J Pediatr. 2013 Oct;56(10):456-8. doi: 10.3345/kjp.2013.56.10.456. Epub 2013 Oct 31.
●● Enlace al texto completo (gratuito o de pago) 3345/kjp.2013.56.10.456
AUTORES / AUTHORS: - Kelekci S; Karabel M; Ece A; Sen V; Gunes A; Yolbas I; Sahin C
INSTITUCIÓN / INSTITUTION: - Department of Pediatric Pulmonology, Dicle University Faculty of Medicine, Diyarbakir, Turkey.
RESUMEN / SUMMARY: - Cystic fibrosis (CF) is a genetic disease with autosomal recessive inheritance and is common in Caucasian people. The prevalence of this disease is between ½,000 and 1/3,500 live births, and the incidence varies between populations. Although the CF transmembrane conductance regulator gene is expressed in the kidneys, renal involvement is rare. With advances in the treatment of CF, life expectancy has increased, and some previously unobserved disease associations are now seen in patients with CF. It is important to follow patients with CF for possible abnormalities that may accompany CF. In this paper, we present two rare cases of CF accompanied by nephrotic syndrome.

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[428]
TÍTULO / TITLE: - Occurrence of anaplastic large cell lymphoma following IgG4-related autoimmune pancreatitis and cholecystitis and diffuse large B-cell lymphoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Int J Clin Exp Pathol. 2013 Oct 15;6(11):2560-8.
AUTORES / AUTHORS: - Ishida M; Hodohara K; Yoshida K; Kagotani A; Iwai M; Yoshii M; Okuno H; Horinouchi A; Nakanishi R; Harada A; Yoshida T; Okabe H
INSTITUCIÓN / INSTITUTION: - Department of Clinical Laboratory Medicine, Shiga University of Medical Science Shiga, Japan ; Division of Diagnostic Pathology, Shiga University of Medical Science Shiga, Japan.
RESUMEN / SUMMARY: - IgG4-related sclerosing disease is an established disease entity with characteristic clinicopathological features. Recently, the association between IgG4-related sclerosing disease and the risk of malignancies has been suggested. IgG4-related autoimmune pancreatitis with pancreatic cancer has been reported. Further, a few cases of extraocular malignant lymphoma in patients with IgG4-related sclerosing disease have also been documented. Herein, we describe the first documented case of anaplastic large cell lymphoma (ALCL) following IgG4-related autoimmune pancreatitis and cholecystitis and diffuse large B-cell lymphoma (DLBCL). A 61-year-old Japanese male, with a past history of DLBCL, was detected with swelling of the pancreas and tumorous lesions in the gallbladder. Histopathological study of the resected gallbladder specimen revealed diffuse lymphoplasmacytic infiltration with fibrosclerosis in the entire gallbladder wall. Eosinophilic infiltration and obliterative phlebitis were also noted. Immunohistochemically, many IgG4-positive plasma cells had infiltrated into the lesion, and the ratio of IgG4/IgG-positive plasma cells was 71.6%. Accordingly, a diagnosis of IgG4-related cholecystitis was made. Seven months later, he presented with a painful tumor in his left parotid gland. Histopathological study demonstrated diffuse or cohesive sheet-like proliferation of large-sized lymphoid cells with rich slightly eosinophilic cytoplasm and irregular-shaped large nuclei. These lymphoid cells were positive for CD30, CD4, and cytotoxic markers, but negative for CD3 and ALK. Therefore, a diagnosis of ALK-negative ALCL was made. It has been suggested that the incidence of malignant lymphoma may be high in patients with IgG4-related sclerosing disease, therefore, intense medical follow-up is important in patients with this disorder.

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[429]
TÍTULO / TITLE: - Development and histopathological characterization of tumorgraft models of pancreatic ductal adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Oct 23;8(10):e78183. doi: 10.1371/journal.pone.0078183.
●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0078183
AUTORES / AUTHORS: - Garcia PL; Council LN; Christein JD; Arnoletti JP; Heslin MJ; Gamblin TL; Richardson JH; Bjornsti MA; Yoon KJ
INSTITUCIÓN / INSTITUTION: - Department of Pharmacology and Toxicology, University of Alabama at Birmingham, Birmingham, Alabama, United States of America.
RESUMEN / SUMMARY: - Pancreatic cancer is the one of the deadliest of all malignancies. The five year survival rate for patients with this disease is 3-5%. Thus, there is a compelling need for novel therapeutic strategies to improve the clinical outcome for patients with pancreatic cancer. Several groups have demonstrated for other types of solid tumors that early passage human tumor xenograft models can be used to define some genetic and molecular characteristics of specific human tumors.

Published studies also suggest that murine tumorgraft models (early passage xenografts derived from direct implantation of primary tumor specimens) may be useful in identifying compounds with efficacy against specific tumor types. Because pancreatic cancer is a fatal disease and few well-characterized model systems are available for translational research, we developed and characterized a panel of pancreatic tumorgraft models for biological evaluation and therapeutic drug testing. Of the 41 primary tumor specimens implanted subcutaneously into mice, 35 produced viable tumorgraft models. We document the fidelity of histological and morphological characteristics and of KRAS mutation status among primary (F0), F1, and F2 tumors for the twenty models that have progressed to the F3 generation. Importantly, our procedures produced a take rate of 85%, higher than any reported in the literature. Primary tumor specimens that failed to produce tumorgrafts were those that either contained <10% tumor cells or that were obtained from significantly smaller primary tumors. In view of the fidelity of characteristics of primary tumor specimens through at least the F2 generation in mice, we propose that these tumorgraft models represent a useful tool for identifying critical characteristics of pancreatic tumors and for evaluating potential therapies.

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[430]

TÍTULO / TITLE: - Interactions of Platinum and Ruthenium Coordination Complexes with Pancreatic Phospholipase A2 and Phospholipids Investigated by MALDI TOF Mass Spectrometry.

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

REVISTA / JOURNAL: - Chem Biodivers. 2013 Nov;10(11):1972-86. doi: 10.1002/cbdv.201300141.

●● Enlace al texto completo (gratuito o de pago) 1002/cbdv.201300141

AUTORES / AUTHORS: - Kamceva T; Radisavljevic M; Vukicevic I; Arnhold J; Petkovic M

INSTITUCIÓN / INSTITUTION: - 'Vinca' Institute of Nuclear Sciences, Department of Physical Chemistry, University of Belgrade, Mike Petrovica Alasa 12-14, RS-11001 Belgrade (phone: +381 11 3408 64; fax: +381 11 8066 434); Haukeland University Hospital, Laboratory of Clinical Biochemistry, Section of Clinical Pharmacology, Jonas Lies Vei 65, NO-5020 Bergen (phone: +47 46 572612; fax:+47 55 290 718). tina@vinca.rs.

RESUMEN / SUMMARY: - Phospholipase A2 is involved in propagation of inflammatory processes and carcinogenesis through its role in phospholipid metabolism, and release of arachidonic acid and lysophospholipids. Recent findings on correlation between elevated PLA2 activity and metastatic cancer render this enzyme an attractive target for cancer therapy. On the other hand, due to a broad range of oxidation states under physiological conditions and a high affinity for protein binding, platinum and ruthenium coordination complexes are promising candidates for PLA2 inhibitors. In this article, we discuss the interactions of Pt and Ru coordination complexes with PLA2 and phospholipids, as well as the application of MALDI-TOF mass spectrometry for screening PLA2 inhibitors. Owing to the ability of this technique to simultaneously detect and monitor changes in substrate and product concentrations, the inhibitor mechanisms of both Pt and Ru complexes with various ligands were determined.

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[431]

TÍTULO / TITLE: - Insulinoma presenting with cardiac arrest and cardiomyopathy.
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

●● Cita: British Medical J. (BMJ): <> Case Rep. 2013 Oct 23;2013. pii: bcr2013009193. doi: 10.1136/bcr-2013-009193.

●● Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-009193

AUTORES / AUTHORS: - Thirumalai A; Levander XA; Mookherjee S; White AA
INSTITUCIÓN / INSTITUTION: - Internal Medicine Residency Program, University of Washington, Seattle, Washington, USA.
RESUMEN / SUMMARY: - A 33-year-old woman presented with ventricular fibrillation cardiac arrest and was found to have a blood glucose of 1.83 mmol/L. Cardiac catheterisation revealed a dilated left ventricle with an ejection fraction (EF) of 26% and angiographically normal coronary arteries. Continuous dextrose infusion was required to treat hypoglycaemia, which prompted consideration of insulinoma as a possible cause for her cardiomyopathy. Whipple's triad was demonstrated; a 72 h fast provided biochemical evidence of insulinoma, and imaging localised a tumour in her pancreas. The tumour was resected and pathology confirmed insulinoma; pancreaticoduodenectomy cured her hypoglycaemia. No alternate cause of cardiomyopathy was found and 4 months after surgery her EF improved to 41%. High insulin levels can close cardiac KATP channels associated with dilated cardiomyopathy; the catecholamine surge from hypoglycaemia may also contribute to ventricular remodelling. Hypoglycaemia can cause QT segment prolongation, and may have precipitated fibrillation in this patient's arrhythmia-prone myocardium.

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[432]
TÍTULO / TITLE: - Can DCE-MRI Explain the Heterogeneity in Radiopeptide Uptake Imaged by SPECT in a Pancreatic Neuroendocrine Tumor Model?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Oct 8;8(10):e77076. doi: 10.1371/journal.pone.0077076.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0077076

AUTORES / AUTHORS: - Bol K; Haeck JC; Groen HC; Niessen WJ; Bernsen MR; de Jong M; Veenland JF
INSTITUCIÓN / INSTITUTION: - Biomedical Imaging Group Rotterdam, Departments of Radiology and Medical Informatics, Erasmus Medical Center, Rotterdam, The Netherlands ; Department of Radiology, Erasmus Medical Center, Rotterdam, The Netherlands ; Department of Nuclear Medicine, Erasmus Medical Center, Rotterdam, The Netherlands.
RESUMEN / SUMMARY: - Although efficient delivery and distribution of treatment agents over the whole tumor is essential for successful tumor treatment, the distribution of most of these agents cannot be visualized. However, with single-photon emission computed tomography (SPECT), both delivery and uptake of radiolabeled peptides can be visualized in a neuroendocrine tumor model overexpressing somatostatin receptors. A heterogeneous peptide uptake is often observed in these tumors. We hypothesized that peptide distribution in the tumor is spatially related to tumor perfusion, vessel density and permeability, as imaged and quantified by DCE-MRI in a neuroendocrine tumor model. Four subcutaneous CA20948 tumor-bearing Lewis rats

were injected with the somatostatin-analog (111)In-DTPA-Octreotide (50 MBq). SPECT-CT and MRI scans were acquired and MRI was spatially registered to SPECT-CT. DCE-MRI was analyzed using semi-quantitative and quantitative methods. Correlation between SPECT and DCE-MRI was investigated with 1) Spearman's rank correlation coefficient; 2) SPECT uptake values grouped into deciles with corresponding median DCE-MRI parametric values and vice versa; and 3) linear regression analysis for median parameter values in combined datasets. In all tumors, areas with low peptide uptake correlated with low perfusion/density/ /permeability for all DCE-MRI-derived parameters. Combining all datasets, highest linear regression was found between peptide uptake and semi-quantitative parameters ($R(2)>0.7$). The average correlation coefficient between SPECT and DCE-MRI-derived parameters ranged from 0.52-0.56 ($p<0.05$) for parameters primarily associated with exchange between blood and extracellular extravascular space. For these parameters a linear relation with peptide uptake was observed. In conclusion, the 'exchange-related' DCE-MRI-derived parameters seemed to predict peptide uptake better than the 'contrast amount- related' parameters. Consequently, fast and efficient diffusion through the vessel wall into tissue is an important factor for peptide delivery. DCE-MRI helps to elucidate the relation between vascular characteristics, peptide delivery and treatment efficacy, and may form a basis to predict targeting efficiency.

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[433]

TÍTULO / TITLE: - Ischemic stroke as a presenting feature of VIPoma due to MEN 1 syndrome.

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

REVISTA / JOURNAL: - Indian J Endocrinol Metab. 2013 Oct;17(Suppl 1):S215-8. doi: 10.4103/2230-8210.119576.

●● Enlace al texto completo (gratuito o de pago) 4103/2230-8210.119576

AUTORES / AUTHORS: - Maheshwari RR; Desai M; Rao VP; Palanki RR; Namburi RP; Reddy KT; Reddy AP

INSTITUCIÓN / INSTITUTION: - Department of Endocrinology and Metabolism, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India.

RESUMEN / SUMMARY: - INTRODUCTION: Presentation of the ischemic stroke due to vasoactive intestinal peptide producing tumor (VIPoma) or Verner Morrison syndrome is rare. This is first of its kind case which we are reporting here which was later turned out to be multiple endocrine neoplasia type 1 (MEN 1) syndrome with diagnosis of primary hyperparathyroidism in the same patient in follow-up. DESCRIPTION OF THE CASE: A 13-year-old girl presented to our emergency department with features of disorientation, weakness of left sided extremities. She had watery high volume diarrhea and related dehydration with renal failure. Blood chemistry was suggestive of hypokalemia with metabolic acidosis. Patient had flushing on her face during this episode of illness. Magnetic resonance imaging (MRI) of brain suggested venous infarct. Computed tomography (CT) scan of abdomen done with high index of suspicion was suggestive of mass in tail of pancreas mostly a VIPoma. Patient was operated for the tumor after which there was no recurrence of diarrhea. Biopsy of tumor was consistent with VIPoma with chomogranin A positivity. Patient improved of her stroke episode with time. On follow-up she is diagnosed to have primary hyperparathyroidism with hypercalcemia due to left inferior parathyroid adenoma which improved with intravenous (IV) zolindronic acid therapy and now she is planned to undergo

parathyroidectomy. CONCLUSION: VIPoma is a rare tumor but is well-described with MEN 1. Stroke as a presenting feature of VIPoma is first reported with this case.

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[434]

TÍTULO / TITLE: - Further Characterization of the Target of a Potential Aptamer Biomarker for Pancreatic Cancer: Cyclophilin B and Its Posttranslational Modifications.

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

REVISTA / JOURNAL: - Nucleic Acid Ther. 2013 Oct 23.

●● Enlace al texto completo (gratuito o de pago) 1089/nat.2013.0439

AUTORES / AUTHORS: - Ray P; Sullenger BA; White RR

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Duke University School of Medicine , Durham, North Carolina.

RESUMEN / SUMMARY: - Posttranslational modifications on proteins can serve as useful biomarkers for disease. However, their discovery and detection in biological fluids is challenging. Aptamers are oligonucleotide ligands that demonstrate high affinity toward their target proteins and can discriminate closely related proteins with superb specificity. Previously, we generated a cyclophilin B aptamer (M9-5) that could discriminate sera from pancreatic cancer patients and healthy volunteers with high specificity and sensitivity. In our present work we further characterize the aptamer and the target protein, cyclophilin B, and demonstrate that the aptamer could discriminate between cyclophilin B expressed in human cells versus bacteria. Using mass-spectrometric analysis, we discovered post-translational modifications on cyclophilin B that might be responsible for the M9-5 selectivity. The ability to distinguish between forms of the same protein with differing post-translational modifications is an important advantage of aptamers as tools for identification and detection of biomarkers.

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[435]

TÍTULO / TITLE: - Abraxane approved for metastatic pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Discov. 2013 Nov;3(11):OF3. doi: 10.1158/2159-8290.CD-NB2013-137. Epub 2013 Sep 26.

●● Enlace al texto completo (gratuito o de pago) 1158/2159-8290.CD-NB2013-137

RESUMEN / SUMMARY: - The U.S. Food and Drug Administration, in September 2013, approved the use of Abraxane in combination with gemcitabine to treat patients with late-stage pancreatic cancer.

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[436]

TÍTULO / TITLE: - Folate-chitosan-gemcitabine core-shell nanoparticles targeted to pancreatic cancer.

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

REVISTA / JOURNAL: - Chin J Cancer Res. 2013 Oct;25(5):527-535.

●● Enlace al texto completo (gratuito o de pago) 3978/j.issn.1000-9604.2013.09.04

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RESUMEN / SUMMARY: - OBJECTIVE: Human pancreatic cancer is one of the most common clinical malignancies. The effect of comprehensive treatment based on surgery is general. The effects of chemotherapy were not obvious mainly because of lack of targeting and chemoresistance in pancreatic cancer. This study aimed to investigate the effects of folate receptor (FR)-mediated gemcitabine FA-Chi-Gem nanoparticles with a core-shell structure by electrostatic spray on pancreatic cancer. METHODS: In this study, the levels of expression of FR in six human pancreatic cancer cell lines were studied by immunohistochemical analysis. The uptake rate of isothiocyanate-labeled FA-Chi nanoparticles in FR high expression cell line COLO357 was assessed by fluorescence microscope and the inhibition rate of FA-Chi-Gem nanoparticles on COLO357 cells was evaluated by MTT assay. Moreover, the biodistribution of PEG-FA-ICGDER02-Chi in the orthotopic pancreatic tumor model was observed using near-infrared imaging and the human pancreatic cancer orthotopic xenografts were treated with different nanoparticles and normal saline control. RESULTS: The expression of FR in COLO357 was the highest among the six pancreatic cancer cell lines. The FR mainly distributed on cell membrane and fewer in the cytoplasm in pancreatic cancer. Moreover, the absorption rate of the FA-Chi-Gem nanoparticles was more than the Chi nanoparticles without FA modified. The proliferation of COLO357 was significantly inhibited by FA-Chi-Gem nanoparticles. The PEG-FA-ICGDER02-Chi nanoparticles were enriched in tumor tissue in human pancreatic cancer xenografts, while non-targeted nanoparticles were mainly in normal liver tissue. PEG-FA-Gem-Chi significantly inhibited the growth of human pancreatic cancer xenografts (PEG-FA-Gem-Chi vs. Gem, t=22.950, P=0.000). CONCLUSIONS: PEG-FA-FITC-Chi nanoparticles might be an effective targeted drug for treating human FR-positive pancreatic cancer.
