

#01#

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

Pancreatic cancer.

Agosto - Septiembre 2013 / August - September 2013

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[1]

TÍTULO / TITLE: - Modular Microsystem for the Isolation, Enumeration, and Phenotyping of Circulating Tumor Cells in Patients with Pancreatic Cancer.

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

REVISTA / JOURNAL: - Anal Chem. 2013 Oct 1;85(19):9092-9100. Epub 2013 Sep 10.

●● Enlace al texto completo (gratis o de pago) [1021/ac401720k](#)

AUTORES / AUTHORS: - Hupert ML; Witek MA; Wang H; Torphy RJ; Dharmasiri U; Njoroge SK; Jackson JM; Aufforth RD; Snavely A; Yeh JJ; Soper SA

INSTITUCIÓN / INSTITUTION: - Department of Chemistry, Louisiana State University , 232 Choppin Hall, Baton Rouge, Louisiana 70803-1804, United States.

RESUMEN / SUMMARY: - In this manuscript, we discuss the development and clinical use of a thermoplastic modular microsystem for the high-throughput analysis of CTCs directly from whole blood. The modular system offers some innovative features that address challenges currently associated with many CTC platforms; it can exhaustively process 7.5 mL of blood in less than 45 min with recoveries >90%. In addition, the system automates the postselection CTC processing steps and thus, significantly reduces assay turnaround time (from selection to enumeration <1.5 h as compared to >8 h for many reported CTC platforms). The system is composed of 3 functional modules including (i) a thermoplastic CTC selection module composed of high aspect ratio (30 µm x 150 µm) channels containing anti-EpCAM antibodies that is scalable in terms of throughput by employing channel numbers ranging from 50 to 320; the

channel number is user selected to accommodate the volume of blood that must be processed; (ii) an impedance sensor module for label-less CTC counting; and (iii) a staining and imaging module for the placement of released cells into a 2D array within a common imaging plane for phenotypic identification. To demonstrate the utility of this system, blood samples from patients with local resectable and metastatic pancreatic ductal adenocarcinoma (PDAC) were analyzed. We demonstrate the ability to select EpCAM positive CTCs from PDAC patients in high purity (>86%) and with excellent yields (mean = 53 CTCs per mL for metastatic PDAC patients) using our modular system. In addition, we demonstrate the ability to detect CTCs in PDAC patients with local resectable disease (mean = 11 CTCs per mL).

TÍTULO / TITLE: - Pancreatic adenocarcinoma in duodenal ectopic pancreas: a case report and review of the literature.

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

REVISTA / JOURNAL: - Pathologica. 2013 Apr;105(2):56-8.

AUTORES / AUTHORS: - Ginori A; Vassallo L; Butorano MA; Bettarini F; Di Mare G; Marrelli D

INSTITUCIÓN / INSTITUTION: - Department of Medical Biotechnology, Section of Anatomical Pathology, University of Siena, Siena, Italy. ginori@student.unisi.it

RESUMEN / SUMMARY: - Ectopic pancreas is defined as pancreatic tissue outside the normal location without connection to the normal pancreas. It occurs throughout the gastrointestinal tract, most commonly in the stomach (25-60%), followed by the duodenum (25-35%) and jejunum (16%). It may develop the same pathological changes of a normal pancreas such as acute pancreatitis and cyst formation. Malignant degeneration rarely occurs. We present a case of heterotopic pancreatic adenocarcinoma localized in the duodenal bulb presenting with symptoms of gastric obstruction.

[2]

TÍTULO / TITLE: - Comparison of MUC4 expression in primary pancreatic cancer and paired lymph node metastases.

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

REVISTA / JOURNAL: - Scand J Gastroenterol. 2013 Oct;48(10):1183-7. doi: 10.3109/00365521.2013.832368.

●● [Enlace al texto completo \(gratis o de pago\) 3109/00365521.2013.832368](#)

AUTORES / AUTHORS: - Ansari D; Urey C; Gundewar C; Bauden MP; Andersson R

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Clinical Sciences Lund, Lund University, and Skane University Hospital, Lund, Sweden.

RESUMEN / SUMMARY: - Abstract Objective. Mucin 4 (MUC4) is a transmembrane glycoprotein that is expressed in pancreatic ductal adenocarcinoma (PDAC), but not in normal pancreatic tissue. MUC4 has a proposed role in pancreatic tumor progression and metastasis. The purpose of this pilot study was to investigate MUC4 expression during PDAC metastasis by comparing the expression in the primary tumor and paired lymph node metastases from the same patient. Material and methods. Surgical specimens from 17 cases of primary PDAC and paired lymph node metastases were immunohistochemically analyzed for MUC4 expression. The modified histochemical score (H-score) was used for staining assessment. Results. Positive staining for MUC4 was detected in most primary and metastatic PDAC tumors (15/17 vs. 14/17). The concordance for MUC4 expression in primary tumors and corresponding lymph node metastases was 82%. In two cases, the primary tumor was MUC4-positive and the lymph node metastases were negative, while in one patient with a MUC4-negative primary tumor, the lymph node metastasis was positive. The distribution of H-score for expression of MUC4 significantly correlated ($r = 0.615$; $p = 0.009$) between primary tumors and paired metastatic lesions. Conclusions: MUC4 was observed in both primary and matched metastatic tumors with a high level of concordance, suggesting that MUC4 expression is retained following PDAC metastasis.

TÍTULO / TITLE: - The Addition of Radiation to Chemotherapy does not Improve Outcome When Compared to Chemotherapy in the Treatment of Resected Pancreas Cancer: The Results of a Single-Institution Experience.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Sep 18.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3266-1](#)

AUTORES / AUTHORS: - Martin LK; Luu DC; Li X; Muscarella P; Christopher Ellison E; Bloomston M; Bekaii-Saab T

INSTITUCIÓN / INSTITUTION: - Division of Medical Oncology, Department of Internal Medicine, The Ohio State University, Columbus, OH, USA.

RESUMEN / SUMMARY: - BACKGROUND: Pancreas cancer is highly lethal even at early stages. Adjuvant therapy with chemotherapy (CT) or chemoradiation (CRT) is standard following surgery to delay recurrence and improve survival. There is no consensus on the added value of radiotherapy (RT). We conducted a retrospective analysis of clinical outcomes in pancreas cancer patients treated with CT or CRT following surgery. METHODS: Patients with resected pancreas adenocarcinoma were identified in our institutional database. Relevant clinicopathologic and demographic data were collected. Patients were grouped according to adjuvant treatment: group A: no treatment; group B: CT; group C: CRT. The primary endpoint of overall survival was compared between groups B vs. C. Univariate and multivariate analyses of potential prognostic factors were conducted including all patients. RESULTS: A total of 146

evaluable patients were included (group A: n = 33; group B: n = 45; group C: n = 68). Demographics and pathologic characteristics were comparable. There was no significant survival benefit for CRT compared with CT (mOS 16.8 months vs. 21.5 months, respectively, p = 0.76). Local recurrence rates were similar in all three groups. Univariate analyses identified absence of lymph node involvement (hazards ratio [HR] 1.43, p = 0.0082) and administration of adjuvant therapy (HR 0.496, p = 0.0008) as significant predictors for improved survival. Multivariate analyses suggested that patients without nodal involvement derived the most benefit from adjuvant treatment. CONCLUSIONS: The addition of RT to CT did not improve survival over CT. Lymph node involvement predicts inferior clinical outcome.

[3]

TÍTULO / TITLE: - Pancreatic cancer clinical trials and accrual in the United States.

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

REVISTA / JOURNAL: - J Clin Oncol. 2013 Sep 20;31(27):3432-8. doi: 10.1200/JCO.2013.49.4823. Epub 2013 Aug 19.

●● Enlace al texto completo (gratis o de pago) [1200/JCO.2013.49.4823](https://doi.org/10.1200/JCO.2013.49.4823)

AUTORES / AUTHORS: - Hoos WA; James PM; Rahib L; Talley AW; Fleshman JM; Matrisian LM

INSTITUCIÓN / INSTITUTION: - All authors: Pancreatic Cancer Action Network, Manhattan Beach, CA.

RESUMEN / SUMMARY: - PURPOSE: Pancreatic cancer clinical trials open in the United States and their accrual were examined to identify opportunities to accelerate progress in the treatment of pancreatic cancer. METHODS: Pancreatic cancer-specific clinical trials open in the United States in the years 2011 and 2012 were obtained from the Pancreatic Cancer Action Network database. Accrual information was obtained from trial sponsors. RESULTS: The portfolio of pancreatic cancer clinical trials identified by type (adenocarcinoma or neuroendocrine), phase, disease stage, and treatment approach is reported. More than half of trials for patients with pancreatic ductal adenocarcinoma applied biologic insights to new therapeutic approaches, and 38% focused on optimization of radiation or chemotherapy delivery or regimens. In 2011, pancreatic cancer trials required total enrollment of 11,786 patients. Actual accrual to 93.2% of trials was 1,804 patients, an estimated 4.57% of the patients with pancreatic cancer alive in that year. The greatest need was for patients with resectable cancer. Trials open in 2011 enrolled an average of 15% of their total target accrual. Physician recommendations greatly influenced patients' decision to enroll or not enroll onto a clinical trial. Matching to a clinical trial within a 50-mile radius and identifying trials for recurrent/refractory disease were documented as challenges for patient accrual. CONCLUSION: Overall trial enrollment indicates that pancreatic cancer trials open in 2011 would require 6.7 years on average to complete accrual. These results

suggest that harmonizing patient supply and demand for clinical trials is required to accelerate progress toward improving survival in pancreatic cancer.

[4]

TÍTULO / TITLE: - Phase II trial of gemcitabine and S-1 for patients with advanced pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Oct;72(4):845-52. doi: 10.1007/s00280-013-2265-z. Epub 2013 Aug 27.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2265-z](#)

AUTORES / AUTHORS: - Song H; Han B; Park CK; Kim JH; Jeon JY; Kim IG; Kim HJ; Jung JY; Kim JH; Kwon JH; Jang G; Kim HY; Kim HS; Choi DR; Zang DY

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Hallym University Medical Center, Hallym University College of Medicine, #170 Gwanpyeng-ro, Dongahn gu, Anyang, GyeongGi-Do, 431-070, Republic of Korea.

RESUMEN / SUMMARY: - PURPOSE: To evaluate the efficacy and safety of combined gemcitabine and S-1 as first-line chemotherapy for patients with locally advanced or metastatic pancreatic cancer. METHODS: This study included patients who had been diagnosed with unresectable, locally advanced or metastatic adenocarcinoma arising from the pancreas, which was histologically or cytologically confirmed and involved at least 1 unidimensionally measurable lesion. The regimen consisted of intravenous 1,000 mg/m² gemcitabine on day 1 and 8 combined with oral S-1 on days 1-14 every 21 days. The dosage of S-1 was based on the body surface area (BSA) as follows: 40 mg bid (total 80 mg/day) for a BSA of <1.25, 50 mg bid (total 100 mg/day) for a BSA of ≥ 1.25 but <1.5, and 60 mg bid (total 120 mg/day) for a BSA of ≥ 1.5 . Treatment consisted of at least 2 courses unless rapid disease progression was noted. The primary end points were the response and disease control rates, and the secondary end points were toxicity and survival. RESULTS: Thirty-seven patients were enrolled between August 2005 and December 2010. The median number of chemotherapy cycles was 4 (range 1-28 cycles). Response to treatment could be evaluated in 31 patients. None of the patients showed complete response, but 5 achieved partial response. The response rate was thus 13.5 % [95 % confidence interval (CI) 2.7-24.3 %] in the intent-to-treat population. Sixteen patients (43.2 %; 95 % CI 27-59.5 %) showed stable disease, and the overall disease control rate was 56.8 % (95 % CI 40.6-72.9 %). For all 37 patients, the median progression-free survival was 4.6 months (95 % CI 1.8-7.6 month), and the median overall survival was 9.4 month (95 % CI 5.8-12.6 month). Chemotherapy-related grade $\frac{3}{4}$ hematological toxicities were neutropenia (36.1 %), leucopenia (22.2 %), and anemia (13.9 %). The non-hematological toxicities were generally mild. CONCLUSIONS: Combination chemotherapy with gemcitabine and S-1 was effective, convenient, and safe in patients with advanced pancreatic cancer.

[5]

TÍTULO / TITLE: - Updated long-term outcomes and prognostic factors for patients with unresectable locally advanced pancreatic cancer treated with intraoperative radiotherapy at the Massachusetts General Hospital, 1978 to 2010.

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

REVISTA / JOURNAL: - Cancer. 2013 Sep 4. doi: 10.1002/cncr.28329.

●● Enlace al texto completo (gratis o de pago) [1002/cncr.28329](#)

AUTORES / AUTHORS: - Cai S; Hong TS; Goldberg SI; Fernandez-Del Castillo C; Thayer SP; Ferrone CR; Ryan DP; Blaszkowsky LS; Kwak EL; Willett CG; Lillemoe KD; Warshaw AL; Wo JY

INSTITUCIÓN / INSTITUTION: - Harvard Medical School, Boston, Massachusetts.

RESUMEN / SUMMARY: - BACKGROUND: In the current study, the authors evaluated long-term outcomes, intraoperative radiotherapy (IORT)-related toxicity, and prognostic factors for overall survival (OS) among patients with unresectable locally advanced pancreatic cancer (LAPC) who received IORT as part of their treatment at the Massachusetts General Hospital (MGH). METHODS: Medical records were reviewed for 194 consecutive patients with unresectable LAPC who were treated with IORT at MGH between 1978 and 2010. OS was calculated using the Kaplan-Meier method. Prognostic factors were evaluated at the univariate level by the log-rank test and at the multivariate level by the Cox proportional hazards model. Rates of disease progression and treatment toxicity were calculated. RESULTS: The 1-year, 2-year, and 3-year survival rates were 49%, 16%, and 6%, respectively. Six patients (3%) survived for > 5 years. The median OS was 12.0 months. Among 183 patients with known post-IORT disease status, the 2-year local progression-free survival and distant metastasis-free survival rates were 41% and 28%, respectively. On multivariate analysis, an IORT applicator diameter \leq 8 cm (hazards ratio [HR], 0.51; 95% confidence interval [95% CI], 0.30-0.84 [P = .009]), a Charlson age-comorbidity index \leq 3 (HR, 0.47; 95% CI, 0.31-0.73 [P = .001]), and receipt of chemotherapy (HR, 0.46; 95% CI, 0.33-0.66 [P < .001]) predicted improved OS. The median OS for patients with all 3 positive prognostic factors was 21.2 months. CONCLUSIONS: Well-selected patients with LAPC with small tumors and low Charlson age-comorbidity indices can achieve good long-term survival outcomes with a treatment regimen that incorporates chemotherapy and IORT. Cancer 2013. © 2013 American Cancer Society.

[6]

TÍTULO / TITLE: - Covered Self-Expandable Metal Stents With an Anti-Migration System Improve Patency Duration Without Increased Complications Compared With

Uncovered Stents for Distal Biliary Obstruction Caused by Pancreatic Carcinoma: A Randomized Multicenter Trial.

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

REVISTA / JOURNAL: - Am J Gastroenterol. 2013 Sep 17. doi: 10.1038/ajg.2013.305.

●● Enlace al texto completo (gratis o de pago) [1038/ajg.2013.305](#)

AUTORES / AUTHORS: - Kitano M; Yamashita Y; Tanaka K; Konishi H; Yazumi S; Nakai Y; Uehara H; Mitoro A; Sanuki T; Takaoka M; Koshitani T; Arisaka Y; Shiba M; Hoki N; Sato H; Sasaki Y; Sato M; Hasegawa K; Kawabata H; Okabe Y; Mukai H

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

RESUMEN / SUMMARY: - **OBJECTIVES:**The requirements of biliary stents used in the palliation of malignant biliary obstruction are a long duration of patency and minimal adverse effects. Covered self-expandable metal stents (SEMSs) have been shown to prevent tumor ingrowth, which is the most frequent complication of uncovered SEMSs. However, because they are prone to migration, the superiority of covered SEMS has yet to be convincingly demonstrated. The aim of this study was to evaluate the superiority of covered over uncovered SEMSs in the palliation of distal biliary obstruction due to unresectable pancreatic carcinoma, using both stent types with relatively low axial force and uncovered flared ends to prevent their migration.**METHODS:**From April 2009 to December 2010, 120 patients who were admitted to 22 tertiary-care centers because of distal biliary obstruction from unresectable pancreatic carcinomas were enrolled in this prospective randomized multicenter study. Patients were randomly assigned to receive a covered or uncovered SEMS deployed at the site of the biliary stricture during endoscopic retrograde cholangiopancreatography. Stent patency time, patient survival time, patient survival time without stent dysfunction (time to stent dysfunction or patient death), cause of stent dysfunction (ingrowth, overgrowth, migration, or sludge formation), and serious adverse events were compared between covered and uncovered SEMS groups.**RESULTS:**Patient survival time in the two groups did not significantly differ (median: 285 and 223 days, respectively; P=0.68). Patient survival time without stent dysfunction was significantly longer in the covered than in the uncovered SEMS group (median: 187 vs. 132 days; P=0.043). Stent patency was also significantly longer in the covered than in the uncovered SEMS group (mean+/-s.d.: 219.3+/-159.1 vs. 166.9+/-124.9 days; P=0.047). Reintervention for stent dysfunction was performed in 14 of 60 patients with covered SEMSs (23%) and in 22 of 60 patients with uncovered SEMSs (37%; P=0.08). Stent dysfunction was caused by tumor ingrowth, tumor overgrowth, and sludge formation in 0 (0%), 3 (5%), and 11 (18%) patients in the covered SEMSs group, and in 15 (25%), 2 (3%), and 6 (10%) patients in the uncovered SEMSs group, respectively. Stent migration was not observed in either group. Rates of tumor overgrowth and sludge formation did not significantly differ between the two groups, whereas the rate of tumor ingrowth was significantly lower in the covered than in the

uncovered SEMS group ($P < 0.01$). Acute pancreatitis occurred in only one patient in the covered SEMS group. Acute cholecystitis occurred in one patient in the covered SEMS group and in two patients in the uncovered SEMS group. There was no significant difference between the two groups in the incidence of serious adverse events. CONCLUSIONS: By preventing tumor ingrowth and migration, covered SEMSs with an anti-migration system had a longer duration of patency than uncovered SEMSs, which recommends their use in the palliative treatment of patients with biliary obstruction due to pancreatic carcinomas. Am J Gastroenterol advance online publication, 17 September 2013; doi:10.1038/ajg.2013.305.

[7]

TÍTULO / TITLE: - A randomized controlled trial of gemcitabine plus cisplatin versus gemcitabine alone in the treatment of metastatic pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Sep;72(3):637-42. doi: 10.1007/s00280-013-2239-1. Epub 2013 Aug 3.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2239-1](#)

AUTORES / AUTHORS: - Chao Y; Wu CY; Wang JP; Lee RC; Lee WP; Li CP

INSTITUCIÓN / INSTITUTION: - Cancer Center, Taipei Veterans General Hospital, Taipei, Taiwan.

RESUMEN / SUMMARY: - PURPOSE: To compare the efficacy and toxicity of single-agent gemcitabine with gemcitabine plus cisplatin (G + C) in patients with metastatic pancreatic cancer METHODS: Forty-six patients with metastatic pancreatic cancer were randomized to receive gemcitabine alone ($n = 25$; 1,000 mg m^{-2}) or G + C ($n = 21$; 1,000 mg m^{-2} gemcitabine and 25 mg m^{-2} cisplatin). Treatments were administered once a week for 3 weeks and repeated every 4 weeks. RESULTS: Patient characteristics were comparable between the gemcitabine alone and G + C groups. The gemcitabine dose intensity was similar between the gemcitabine alone and G + C groups (684 \pm 32 vs. 617 \pm 31 mg m^{-2} week $^{-1}$). The cisplatin dose intensity was 15.1 \pm 0.9 mg m^{-2} week $^{-1}$ \times 9.9 \pm 1.8 weeks. Partial response rates were 8 % (2/25) for gemcitabine alone and 4.8 % (1/21) for G + C ($p = 1$). The median survival and median time to progression were 7.7 and 4.6 months for gemcitabine alone and 7.9 and 3.6 months for G + C, respectively ($p = 0.752$ and $p = 0.857$, respectively). Clinical benefit was 36 % for gemcitabine alone and 29 % for G + C ($p = 0.592$). Quality-adjusted life months were 5.6 \pm 0.3 for the gemcitabine alone group and 3.8 \pm 0.2 for the G + C group ($p < 0.001$). The frequency of grade ≥ 3 neutropenia (8 vs. 19 %) and anemia (8 vs. 10 %) and the number of hospitalization days per month of survival (4.7 \pm 1.3 vs. 6.3 \pm 1.6 days; $p = 0.431$) were not significantly different between patients who received gemcitabine alone and those who received G + C. However, patients in the G + C group had a higher rate of thrombocytopenia than did patients in the

gemcitabine alone group (62 vs. 24 %; $p = 0.009$). CONCLUSIONS: Gemcitabine alone and G + C had comparable and modest response rates in metastatic pancreatic cancer, but gemcitabine alone produced less toxicities than did G + C.

[8]

TÍTULO / TITLE: - Maintenance sunitinib or observation in metastatic pancreatic adenocarcinoma: A phase II randomised trial.

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

REVISTA / JOURNAL: - Eur J Cancer. 2013 Jul 27. pii: S0959-8049(13)00545-5. doi: 10.1016/j.ejca.2013.06.041.

●● Enlace al texto completo (gratis o de pago) 1016/j.ejca.2013.06.041

AUTORES / AUTHORS: - Reni M; Cereda S; Milella M; Novarino A; Passardi A; Mambrini A; Di Lucca G; Aprile G; Belli C; Danova M; Bergamo F; Franceschi E; Fugazza C; Ceraulo D; Villa E

INSTITUCIÓN / INSTITUTION: - S. Raffaele Scientific Institute, Milan, Italy. Electronic address: reni.michele@hsr.it.

RESUMEN / SUMMARY: - BACKGROUND: New strategies to prolong disease control warrant investigation in patients with metastatic pancreatic adenocarcinoma. This open-label, randomised, multi-centre phase II trial explored the role of maintenance sunitinib after first-line chemotherapy in this setting. METHODS: Patients with pathologic diagnosis of metastatic pancreatic adenocarcinoma, performance status $>50\%$, no progression after 6 months of chemotherapy were centrally randomised by an independent contract research organisation, which was also responsible for data collection and monitoring, to observation (arm A) or sunitinib at 37.5mg daily until progression or a maximum of 6 months (arm B). The primary outcome measure was the probability of being progression-free at 6 months (PFS-6) from randomisation. Assuming $P_0=10\%$; $P_1=30\%$, $\alpha .10$; $\beta .10$, the target accrual was 26 patients per arm. RESULTS: 28 per arm were randomised. One arm B patient had kidney cancer and was excluded. Sunitinib was given for a median of 91 days (7-186). Main grade 3-4 toxicity was thrombocytopenia, neutropenia and hand-foot syndrome (12%), diarrhoea 8%. In arm A versus B, PFS-6 was 3.6% (95% confidence interval (CI): 0-10.6%) and 22.2% (95% CI: 6.2-38.2%; $P<0.01$); 2y overall survival was 7.1% (95% CI: 0-16.8%) and 22.9% (95% CI: 5.8-40.0%; $P=0.11$), stable disease 21.4% and 51.9% ($P=0.02$). CONCLUSION: This is the first randomised trial on maintenance therapy in metastatic pancreatic adenocarcinoma. The primary end-point was fulfilled and 2y overall survival was remarkably high, suggesting that maintenance sunitinib is promising and should be further explored in this patient population.

[9]

TÍTULO / TITLE: - Rational Study Endpoint(s) for Preoperative Trials in Pancreatic Cancer: Pathologic Response Rate, Margin Negative Resection, Overall Survival or 'All of the Above'?

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Aug 14.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3165-5](#)

AUTORES / AUTHORS: - Varadhachary GR; Evans DB

INSTITUCIÓN / INSTITUTION: - Division of Cancer Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA.

[10]

TÍTULO / TITLE: - MicroRNA 23b Regulates Autophagy Associated With Radioresistance of Pancreatic Cancer Cells.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Aug 2. pii: S0016-5085(13)01138-4. doi: 10.1053/j.gastro.2013.07.048.

●● Enlace al texto completo (gratis o de pago) [1053/j.gastro.2013.07.048](#)

AUTORES / AUTHORS: - Wang P; Zhang J; Zhang L; Zhu Z; Fan J; Chen L; Zhuang L; Luo J; Chen H; Liu L; Chen Z; Meng Z

INSTITUCIÓN / INSTITUTION: - Department of Integrative Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Tumor resistance to radiation is a challenge in the treatment of patients with pancreatic cancer. Improving our understanding of the mechanisms of radioresistance could lead to strategies to increase patients' response to therapy. We investigated the roles of microRNAs (miRNAs) involved in radioresistance of pancreatic cancer cells. METHODS: We established radioresistant pancreatic cancer cell lines and used array analysis to compare levels of different miRNAs between radioresistant cell lines and the parental cell lines from which they were derived. We transfected pancreatic cancer cells with miRNA mimics or inhibitors and evaluated their effects on cell radiosensitivity using a clonogenic survival assay. The effects of miRNA on autophagy were determined by transmission electron microscopy and immunoblot analysis. We used a luciferase reporter assay to identify messenger RNA targets of specific miRNAs. RESULTS: Radioresistant pancreatic cancer cells had reduced levels of the miRNA miR-23b and increased autophagy compared with cells that were not radioresistant. Overexpression of miR-23b inhibited radiation-induced autophagy, whereas an inhibitor of miR-23b promoted autophagy in pancreatic cancer cells. Overexpression of miR-23b sensitized pancreatic cancer cells to radiation. The target of miR-23b, ATG12, was overexpressed in radioresistant cells; levels of ATG12 protein correlated with the occurrence of

autophagy. Expression of miR-23b blocked radiation-induced autophagy and sensitized pancreatic cancer cells to radiation. We observed an inverse correlation between the level of miR-23b and autophagy in human pancreatic cancer tissue samples.

CONCLUSIONS: In pancreatic cancer cells, reduced levels of the miRNA miR-23b increase levels of ATG12 and autophagy to promote radioresistance. miR-23b might be used to increase the sensitivity of pancreatic cancer cells to radiation therapy.

[11]

TÍTULO / TITLE: - The Healthy Eating Index 2005 and Risk for Pancreatic Cancer in the NIH-AARP Study.

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

REVISTA / JOURNAL: - J Natl Cancer Inst. 2013 Sep 4;105(17):1298-305. doi: 10.1093/jnci/djt185. Epub 2013 Aug 15.

●● [Enlace al texto completo \(gratis o de pago\) 1093/jnci/djt185](#)

AUTORES / AUTHORS: - Arem H; Reedy J; Sampson J; Jiao L; Hollenbeck AR; Risch H; Mayne ST; Stolzenberg-Solomon RZ

INSTITUCIÓN / INSTITUTION: - Affiliations of authors: Yale School of Public Health, New Haven, CT (HA, HR, STM); Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD (HA, JS, RZS-S); Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD (JR); Baylor College of Medicine, Houston, TX (LJ); AARP, Washington, DC (ARH); Yale Cancer Center, New Haven, CT (HR, STM).

RESUMEN / SUMMARY: - BACKGROUND: Dietary pattern analyses characterizing combinations of food intakes offer conceptual and statistical advantages over food- and nutrient-based analyses of disease risk. However, few studies have examined dietary patterns and pancreatic cancer risk and none focused on the 2005 Dietary Guidelines for Americans. We used the Healthy Eating Index 2005 (HEI-2005) to estimate the association between meeting those dietary guidelines and pancreatic cancer risk. METHODS: We calculated the HEI-2005 score for 537 218 men and women in the National Institutes of Health-American Association of Retired Persons Diet and Health Study using responses to food frequency questionnaires returned in 1995 and 1996. We used Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for risk of pancreatic cancer according to HEI-2005 quintiles and explored effect modification by known risk factors. P interaction values were calculated using the Wald test. All statistical tests were two-sided. RESULTS: We identified 2383 incident, exocrine pancreatic cancer cases (median = 10.5 years follow-up). Comparing participants who met the most dietary guidelines (Q5) with those who met the fewest guidelines (Q1), we observed a reduced risk of pancreatic cancer (HR = 0.85, 95% CI = 0.74 to 0.97). Among men there was an interaction by body mass index (P interaction = .03), with a hazard ratio of 0.72 (95% CI = 0.59 to

0.88) comparing Q5 vs Q1 in overweight/obese men (body mass index $\geq 25\text{kg/m}^2$) but no association among normal weight men. CONCLUSIONS: Our findings support the hypothesis that consuming a high-quality diet, as scored by the HEI-2005, may reduce the risk of pancreatic cancer.

[12]

TÍTULO / TITLE: - Enhanced glucagon-like peptide-1 secretion in a patient with glucagonoma: Implications for glucagon-like peptide-1 secretion from pancreatic alpha cells in vivo.

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

REVISTA / JOURNAL: - Diabetes Res Clin Pract. 2013 Aug 19. pii: S0168-8227(13)00294-5. doi: 10.1016/j.diabres.2013.08.005.

●● Enlace al texto completo (gratis o de pago) [1016/j.diabres.2013.08.005](#)

AUTORES / AUTHORS: - Yabe D; Rokutan M; Miura Y; Komoto I; Usui R; Kuwata H; Watanabe K; Hyo T; Kurose T; Nagamatsu T; Shimizu S; Kawai J; Imamura M; Seino Y

INSTITUCIÓN / INSTITUTION: - Division of Diabetes, Clinical Nutrition and Endocrinology, Kansai Electric Power Hospital, 2-1-7 Fukushima-ku, Osaka 553-0003, Japan; Division of Metabolism and Clinical Nutrition, Kansai Electric Power Hospital, 2-1-7 Fukushima-ku, Osaka 553-0003, Japan. Electronic address: ydaisque-kyoto@umin.ac.jp.

RESUMEN / SUMMARY: - We examined GLP-1 secretion from the pancreas of a patient with glucagonoma and pancreatic resection by measuring GLP-1 after meal ingestion or selective arterial calcium injection, and immunohistochemical analysis. Our findings support the notion that GLP-1 is secreted from pancreatic alpha cells in humans.

[13]

TÍTULO / TITLE: - Macrophage-secreted cytokines drive pancreatic acinar-to-ductal metaplasia through NF-kappaB and MMPs.

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

REVISTA / JOURNAL: - J Cell Biol. 2013 Aug 5;202(3):563-77. doi: 10.1083/jcb.201301001.

●● Enlace al texto completo (gratis o de pago) [1083/jcb.201301001](#)

AUTORES / AUTHORS: - Liou GY; Doppler H; Necela B; Krishna M; Crawford HC; Raimondo M; Storz P

INSTITUCIÓN / INSTITUTION: - Department of Cancer Biology, Mayo Clinic Comprehensive Cancer Center, Mayo Clinic, Jacksonville, FL 32224, USA.

RESUMEN / SUMMARY: - In response to inflammation, pancreatic acinar cells can undergo acinar-to-ductal metaplasia (ADM), a reprogramming event that induces transdifferentiation to a ductlike phenotype and, in the context of additional oncogenic stimulation, contributes to development of pancreatic cancer. The signaling mechanisms underlying pancreatitis-inducing ADM are largely undefined. Our results

provide evidence that macrophages infiltrating the pancreas drive this transdifferentiation process. We identify the macrophage-secreted inflammatory cytokines RANTES and tumor necrosis factor alpha (TNF) as mediators of such signaling. Both RANTES and TNF induce ADM through activation of nuclear factor kappaB and its target genes involved in regulating survival, proliferation, and degradation of extracellular matrix. In particular, we identify matrix metalloproteinases (MMPs) as targets that drive ADM and provide in vivo data suggesting that MMP inhibitors may be efficiently applied to block pancreatitis-induced ADM in therapy.

[14]

TÍTULO / TITLE: - Macrophages in pancreatic cancer: starting things off on the wrong track.

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

REVISTA / JOURNAL: - J Cell Biol. 2013 Aug 5;202(3):403-5. doi: 10.1083/jcb.201307066.

●● Enlace al texto completo (gratis o de pago) [1083/jcb.201307066](#)

AUTORES / AUTHORS: - Deschenes-Simard X; Mizukami Y; Bardeesy N

INSTITUCIÓN / INSTITUTION: - Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA 02114, USA.

RESUMEN / SUMMARY: - Chronic inflammation drives initiation and progression of many malignancies, including pancreatic cancer. In this issue, Liou et al. (2013. J. Cell Biol. [1083/jcb.201301001](#)) report that inflammatory macrophages are major players in the earliest stages of pancreatic cancer. They show that paracrine signals from the macrophages activate the nuclear factor kappaB transcriptional program in normal pancreatic acinar cells, resulting in acinar-ductal metaplasia, a dedifferentiated state that is poised for oncogenic transformation.

[15]

TÍTULO / TITLE: - Retinoblastoma tumor suppressor protein in pancreatic progenitors controls alpha- and beta-cell fate.

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

REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Sep 3;110(36):14723-8. doi: 10.1073/pnas.1303386110. Epub 2013 Aug 14.

●● Enlace al texto completo (gratis o de pago) [1073/pnas.1303386110](#)

AUTORES / AUTHORS: - Cai EP; Wu X; Schroer SA; Elia AJ; Nostro MC; Zacksenhaus E; Woo M

INSTITUCIÓN / INSTITUTION: - Toronto General Research Institute and McEwen Centre for Regenerative Medicine, University Health Network, Toronto, ON, Canada M5G 1L7.

RESUMEN / SUMMARY: - Pancreatic endocrine cells expand rapidly during embryogenesis by neogenesis and proliferation, but during adulthood, islet cells have a very slow turnover. Disruption of murine retinoblastoma tumor suppressor protein (Rb) in mature pancreatic beta-cells has a limited effect on cell proliferation. Here we show that deletion of Rb during embryogenesis in islet progenitors leads to an increase in the neurogenin 3-expressing precursor cell population, which persists in the postnatal period and is associated with increased beta-cell mass in adults. In contrast, Rb-deficient islet precursors, through repression of the cell fate factor aristaless related homeobox, result in decreased alpha-cell mass. The opposing effect on survival of Rb-deficient alpha- and beta-cells was a result of opposing effects on p53 in these cell types. As a consequence, loss of Rb in islet precursors led to a reduced alpha- to beta-cell ratio, leading to improved glucose homeostasis and protection against diabetes.

[16]

TÍTULO / TITLE: - Genetic Alterations Associated With Progression From Pancreatic Intraepithelial Neoplasia to Invasive Pancreatic Tumor.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Aug 2. pii: S0016-5085(13)01139-6. doi: 10.1053/j.gastro.2013.07.049.

●● Enlace al texto completo (gratis o de pago) [1053/j.gastro.2013.07.049](#)

AUTORES / AUTHORS: - Murphy SJ; Hart SN; Lima JF; Kipp BR; Klebig M; Winters JL; Szabo C; Zhang L; Eckloff BW; Petersen GM; Scherer SE; Gibbs RA; McWilliams RR; Vasmataz G; Couch FJ

INSTITUCIÓN / INSTITUTION: - Department of Molecular Medicine, Mayo Clinic, Rochester, Minnesota.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Increasing grade of pancreatic intraepithelial neoplasia (PanIN) has been associated with progression to pancreatic ductal adenocarcinoma (PDAC). However, the mechanisms that control progression from PanINs to PDAC are not well understood. We investigated the genetic alterations involved in this process. METHODS: Genomic DNA samples from laser-capture microdissected PDACs and adjacent PanIN2 and PanIN3 lesions from 10 patients with pancreatic cancer were analyzed by exome sequencing. RESULTS: Similar numbers of somatic mutations were identified in PanINs and tumors, but the mutational load varied greatly among cases. Ten of the 15 isolated PanINs shared more than 50% of somatic mutations with associated tumors. Mutations common to tumors and clonally related PanIN2 and PanIN3 lesions were identified as genes that could promote carcinogenesis. KRAS and TP53 frequently were altered in PanINs and tumors, but few other recurrently modified genes were detected. Mutations in DNA damage response genes were prevalent in all samples. Genes that encode proteins involved in gap junctions, the actin cytoskeleton, the mitogen-activated protein kinase signaling

pathway, axon guidance, and cell-cycle regulation were among the earliest targets of mutagenesis in PanINs that progressed to PDAC. CONCLUSIONS: Early stage PanIN2 lesions appear to contain many of the somatic gene alterations required for PDAC development.

[17]

TÍTULO / TITLE: - Low Accuracy of Tumor Markers for Diagnosing Pancreatic Neuroendocrine Tumors in Multiple Endocrine Neoplasia Type 1 Patients.

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

REVISTA / JOURNAL: - J Clin Endocrinol Metab. 2013 Aug 16.

●● [Enlace al texto completo \(gratis o de pago\) 1210/jc.2013-1800](#)

AUTORES / AUTHORS: - de Laat JM; Pieterman CR; Weijmans M; Hermus AR; Dekkers OM; de Herder WW; van der Horst-Schrivers AN; Drent ML; Bisschop PH; Havekes B; Vriens MR; Valk GD

RESUMEN / SUMMARY: - Context: The assessment of tumor markers for diagnosing pancreatic neuroendocrine tumors (pNET) in multiple endocrine neoplasia type 1 (MEN1) patients is advised in the current guidelines but has never been validated for this purpose. Objective: The objective of the study was to assess the diagnostic accuracy of chromogranin A (CgA), pancreatic polypeptide (PP), and glucagon for pNET in MEN1. Design: This was a diagnostic study. Setting: The study was conducted at Dutch university medical centers from 2008 to 2011, representing 90% of the total Dutch MEN1 population. Patients and Methods: Patients for whom data on tumor markers in combination with the reference standard (ie, radiological imaging) were available between 2008 and 2011 were included. The reference standard for the presence of pNET was pathology or detection on magnetic resonance imaging, computed tomography, or endoscopic ultrasound confirmed on subsequent imaging, irrespective of modality at follow-up. Main Outcome Measures: The area under the receiver-operating characteristic curve (AUC), positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, sensitivity, and specificity were calculated for each marker. Results: For the analysis of PP, CgA, and glucagon, 73, 81, and 94 patients were available, respectively. The AUC for CgA was 0.48 [95% confidence interval (CI) 0.35-0.61] with a sensitivity 0.33 and a specificity 0.73; the AUC for glucagon was 0.58 (95% CI 0.46-0.70) with a sensitivity 0.43 and a specificity 0.73; and the AUC for PP was 0.64 (95% CI 0.50-0.77) with a sensitivity 0.36 and a specificity 0.74. Age, imaging modality, tumor size, and number did not influence the outcomes. Conclusion: The diagnostic accuracy of the tumor markers CgA, PP, and glucagon for pNET in MEN1 is low.

[18]

TÍTULO / TITLE: - Prognostic Factors and Long-Term Outcome of Pancreatic Neuroendocrine Neoplasms: Ki-67 Index Shows a Greater Impact on Survival than Disease Stage. The Large Experience of the Spanish National Tumor Registry (RGETNE).

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

REVISTA / JOURNAL: - Neuroendocrinology. 2013 Sep 19:156-168.

●● Enlace al texto completo (gratis o de pago) [1159/000355152](#)

AUTORES / AUTHORS: - Martin-Perez E; Capdevila J; Castellano D; Jimenez-Fonseca P; Salazar R; Beguiristain-Gomez A; Alonso-Orduna V; Martinez Del Prado P; Villabona-Artero C; Diaz-Perez JA; Monleon A; Marazuela M; Pachon V; Sastre-Valera J; Sevilla I; Castano A; Garcia-Carbonero R

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University Hospital La Princesa, Madrid, España.

RESUMEN / SUMMARY: - Introduction: Pancreatic neuroendocrine neoplasms (PNENs) are uncommon neoplasms with a wide spectrum of clinical behavior. The objective of this study was to assess in a large cohort of patients the relative impact of prognostic factors on survival. Methods: From June 2001 through October 2010, 1,271 patients were prospectively registered online (www.getne.org) at the Spanish National Cancer Registry for Gastroenteropancreatic Neuroendocrine Tumors (RGETNE) by participating centers. Clinical and histopathological features were assessed as potential prognostic factors by uni- and multivariate analyses. Results: Of 483 PNENs, 171 (35%) were functional (F) and 312 (65%) non-functional (NF). NF-PNENs were associated with a higher incidence of histological features denoting more aggressive disease, such as poor tumor differentiation, Ki-67 >20%, or vascular invasion (NF- vs. F-PNENs, respectively, $p < 0.05$). Nevertheless, functionality was not a significant predictor of survival ($p = 0.19$). Stage at diagnosis, Ki-67 index, tumor differentiation and surgical resection of the primary tumor were all significant prognostic factors in univariate analysis. However, Ki-67 (>20 vs. $\leq 2\%$) (hazard ratio (HR) 2.21, $p = 0.01$) and surgical resection (yes vs. no) (HR 0.92, $p = 0.001$) were the only independent predictors of survival in multivariate analysis. Among patients who underwent surgery, high Ki-67 index (HR 10.37, $p = 0.02$) and poor differentiation (HR 8.16, $p = 0.03$) were the only independent predictors of clinical outcome. Conclusion: Ki-67 index and tumor differentiation are key prognostic factors influencing survival of patients with PNENs and, in contrast to what it is observed for other solid malignancies, they seem to have a greater impact on survival than the extent of disease. This should be borne in mind by physicians in order to appropriately tailor therapeutic strategies and surveillance of these patients.

[19]

TÍTULO / TITLE: - Inhibition of amyloid precursor protein processing enhances gemcitabine-mediated cytotoxicity in pancreatic cancer cells.

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

REVISTA / JOURNAL: - J Biol Chem. 2013 Sep 10.

●● Enlace al texto completo (gratis o de pago) [1074/jbc.M113.459255](#)

AUTORES / AUTHORS: - Woods NK; Padmanabhan J

RESUMEN / SUMMARY: - Pancreatic adenocarcinoma or pancreatic cancer is often diagnosed at a very late stage at which point treatment options are minimal. Current chemotherapeutic interventions prolong survival marginally, thereby emphasizing the acute need for better treatment options to effectively manage this disease. Studies from different laboratories have shown that the Alzheimer disease associated Amyloid Precursor Protein (APP) is overexpressed in various cancers but its significance is not known. Here we sought to determine the role of APP in pancreatic cancer cell survival and proliferation. Our results show that pancreatic cancer cells secrete high levels of sAPP-alpha, the alpha-secretase cleaved ectodomain fragment of APP, as compared to normal non-cancerous cells. Treatment of cells with batimastat or GI254023X, inhibitors of the alpha-secretase ADAM10, prevented sAPP-alpha generation and reduced cell survival. Additionally, inhibition of sAPP-alpha significantly reduced anchorage independent growth of the cancer cells. The effect of batimastat on cell survival and colony formation was enhanced when sAPP-alpha downregulation was combined with gemcitabine treatment. Moreover, treatment of batimastat-treated cells with recombinant sAPP-alpha reversed the inhibitory effect of the drug thereby indicating that sAPP-alpha can indeed induce proliferation of cancer cells. Downregulation of APP and ADAM10 brought about similar results, as did batimastat treatment, thereby confirming that APP processing is important for growth and proliferation of these cells. These results suggest that inhibition of sAPP-alpha generation might enhance the effectiveness of the existing chemotherapeutic regimen for a better outcome.

[20]

TÍTULO / TITLE: - Resolution of New-Onset Diabetes After Radical Pancreatic Resection Predicts Long-term Survival in Patients with Pancreatic Ductal Cell Adenocarcinoma.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Aug 14.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3095-2](#)

AUTORES / AUTHORS: - He XY; Li JF; Yao WY; Yuan YZ

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China.

RESUMEN / SUMMARY: - **PURPOSE:** To demonstrate the effect of diabetes mellitus (DM) (stratified by long-term/new-onset presurgical diabetes, resolved/unresolved postsurgical diabetes) on prognosis for pancreatic ductal cell adenocarcinoma (PDAC) after radical resection. **METHODS:** One hundred ninety-nine patients who underwent

radical resection for PDAC between 2007 and 2011 at Ruijin Hospital (Shanghai, China) were retrospectively analyzed. Clinical and pathologic characteristics, surgical and adjuvant chemotherapy related outcomes, disease-free survival (DFS), and postoperative survival were compared among patients with long-term (≥ 2 years)/new-onset (< 2 years) presurgical diabetes and resolved/unresolved postsurgical diabetes. Univariate and multivariable analysis was performed to determine factors associated with DFS and overall survival (OS). RESULTS: Of 199 patients, 90 (44.7 %) had DM, 64 of which were new onset and 26 of which were long-standing. Resolution of DM after radical pancreatic resection was observed in 65 % (42 of 64) in the new-onset group, but in none of the long-standing group. Resolved new-onset DM patients had larger, well-differentiated tumors compared to patients with unresolved new-onset DM. Patients with long-standing DM had shorter postoperative DFS and OS than nondiabetic/new-onset DM, whereas postoperative resolved new-onset DM is associated with longer DFS and OS than unresolved DM. Morbidity was higher and postoperative hospital stay was longer in patients with new-onset DM compared with patients with long-standing DM and patients without DM. There was no difference in the adjuvant chemotherapy toxicity rate among patients with long-standing or new-onset DM and those without DM. CONCLUSIONS: Different status of DM has different effects on outcome after resection for PDAC. Long-standing DM is related to progression of disease, whereas postsurgical resolved new-onset DM is a favorable prognostic factor.

[21]

TÍTULO / TITLE: - VIPoma in a 37-year-old man.

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

REVISTA / JOURNAL: - Lancet. 2013 Aug 31;382(9894):832. doi: 10.1016/S0140-6736(13)61217-9.

●● Enlace al texto completo (gratis o de pago) [1016/S0140-6736\(13\)61217-9](#)

AUTORES / AUTHORS: - Lam S; Liew H; Khor HT; Dalan R; Kon YC; Jong M; Chew DE; Leow MK

INSTITUCIÓN / INSTITUTION: - Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore. stanley_lam@ttsh.com.sg

[22]

TÍTULO / TITLE: - Decreased TIP30 expression predicts poor prognosis in pancreatic cancer patients.

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

REVISTA / JOURNAL: - Int J Cancer. 2013 Sep 5. doi: 10.1002/ijc.28471.

●● Enlace al texto completo (gratis o de pago) [1002/ijc.28471](#)

AUTORES / AUTHORS: - Guo S; Jing W; Hu X; Zhou X; Liu L; Zhu M; Yin F; Chen R; Zhao J; Guo Y

INSTITUCIÓN / INSTITUTION: - International Joint Cancer Research Institute, the Second Military Medical University, 800 Xiangyin Road, Shanghai, 200433, P.R.China; Changhai Hospital, The Second Military Medical University, Shanghai 200433, P.R. China.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is known for its aggressive growth, and is characterized by early tissue invasion and metastasis with poor prognosis. Identifying prognostic markers and delineating the underlying mechanisms that promote progression of PDAC are important for the treatment of pancreatic cancer. TIP30, a newly identified tumor suppressor, appears to be involved in multiple processes during tumor development and metastasis. Here, we investigated the expression of TIP30 in PDAC and its prognostic value in PDAC patients. We examined the expression of TIP30 by immunohistochemistry in tissue microarrays containing 106 surgically resected PDAC. Kaplan-Meier analysis and Cox proportional hazards regression modeling analysis showed that TIP30 expression independently predicted better survival in pancreatectomy patients ($P < 0.01$). Moreover decreased TIP30 expression was associated with lymph node metastasis ($P < 0.05$) and loss of E-cadherin expression ($r = 0.329$, $P < 0.01$). Suppression of TIP30 resulted in up-regulation of Snail and subsequent down-regulation of E-cadherin in SW1990 cells containing high-level of endogenous TIP30. However, in the PANC-1 cells containing low-level of endogenous TIP30, suppressing TIP30 caused up-regulation of Slug instead of Snail, followed by up-regulation of MMP9 rather than E-cadherin. Taken together, the present work reveals that decreased TIP30 expression is able to enhance invasion and metastasis of pancreatic cancer cells through up-regulation of the Snail family members and may serve as an independent predictor for poor outcomes in PDAC patients. © 2013 Wiley Periodicals, Inc.

[23]

TÍTULO / TITLE: - A High-Fat Diet Activates Oncogenic Kras and COX2 to Induce Development of Pancreatic Ductal Adenocarcinoma in Mice.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Aug 16. pii: S0016-5085(13)01191-8. doi: 10.1053/j.gastro.2013.08.018.

●● Enlace al texto completo (gratis o de pago) [1053/j.gastro.2013.08.018](#)

AUTORES / AUTHORS: - Philip B; Roland CL; Daniluk J; Liu Y; Chatterjee D; Gomez SB; Ji B; Huang H; Wang H; Fleming JB; Logsdon CD; Cruz-Monserrate Z

INSTITUCIÓN / INSTITUTION: - Department of Cancer Biology, University of Texas, M. D. Anderson Cancer Center, Houston, TX, USA.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Obesity is a risk factor for pancreatic ductal adenocarcinoma (PDAC), but it is not clear how obesity contributes to

pancreatic carcinogenesis. The oncogenic form of KRAS is expressed during early stages of PDAC development, and is detected in almost all of these tumors. However, there is evidence that mutant KRAS requires an additional stimulus to activate its full oncogenic activity, and that this stimulus involves the inflammatory response. We investigated whether the inflammation induced by a high-fat diet, and accompanying up-regulation of cyclooxygenase-2 (COX2), increases Kras activity during pancreatic carcinogenesis in mice. METHODS: We studied mice with acinar cell-specific expression of KrasG12D (LSL-Kras/Ela-CreERT mice) alone or crossed with COX2 conditional knockout mice (COXKO/LSL-Kras/Ela-CreERT). We also studied LSL-Kras/PDX1-Cre mice. All mice were fed isocaloric diets with different amounts of fat, and a COX2 inhibitor was administered to some LSL-Kras/Ela-CreERT mice. Pancreata were collected from mice and analyzed for Kras activity, levels of phosphorylated ERK, inflammation, fibrosis, pancreatic intraepithelial neoplasia (PanIN), and PDACs. RESULTS: Pancreatic tissues from LSL-Kras/Ela-CreERT mice fed high-fat diets (HFDs) had increased Kras activity, fibrotic stroma, and numbers of PanINs and PDACs than LSL-Kras/Ela-CreERT mice fed control diets; the mice fed the HFDs also had shorter survival times than mice fed control diets. Administration of a COX2 inhibitor to LSL-Kras/Ela-CreERT mice prevented these effects of HFDs. We also observed a significant reduction in survival times of mice fed HFDs. COXKO/LSL-Kras/Ela-CreERT mice fed HFDs had no evidence for increased numbers of PanIN lesions, inflammation, or fibrosis, as opposed to the increases observed in LSL-Kras/Ela-CreERT mice fed HFDs. CONCLUSIONS: In mice, a HFD can activate oncogenic Kras via COX2, leading to pancreatic inflammation and fibrosis, and development of PanINs and PDAC. This mechanism could be involved in the association between risk for PDAC and HFDs.

[24]

TÍTULO / TITLE: - A phase I study of an agonist CD40 monoclonal antibody (CP-870,893) in combination with gemcitabine in patients with advanced pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Sep 4.

●● [Enlace al texto completo \(gratis o de pago\) 1158/1078-0432.CCR-13-1320](#)

AUTORES / AUTHORS: - Beatty GL; Torigian DA; Chiorean EG; Saboury B; Brothers A; Alavi A; Troxel AB; Sun W; Teitelbaum UR; Vonderheide RH; O'Dwyer P

INSTITUCIÓN / INSTITUTION: - Medicine, University of Pennsylvania.

RESUMEN / SUMMARY: - PURPOSE: This phase I study investigated the maximum-tolerated dose (MTD), safety, pharmacodynamics, immunological correlates, and anti-tumor activity of CP-870,893, an agonist CD40 antibody, when administered in combination with gemcitabine in patients with advanced pancreatic ductal adenocarcinoma (PDA). EXPERIMENTAL DESIGN: Twenty-two patients with

chemotherapy-naive advanced PDA were treated with 1000 mg/m² gemcitabine once weekly for 3 weeks with infusion of CP-870,893 at 0.1 mg/kg or 0.2 mg/kg on day 3 of each 28 day cycle. RESULTS: CP-870,893 was well-tolerated; one dose-limiting toxicity (grade 4 cerebrovascular accident) occurred at the 0.2 mg/kg dose level, which was estimated as MTD. The most common adverse event was cytokine release syndrome (grade 1 to 2). CP-870,893 infusion triggered immune activation marked by an increase in inflammatory cytokines, an increase in B cell expression of co-stimulatory molecules, and a transient depletion of B cells. Four patients achieved a partial response (PR). [18F]-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) demonstrated >25% decrease in FDG uptake within primary pancreatic lesions in 6 of 8 patients; however, responses observed in metastatic lesions were heterogeneous with some lesions responding with complete loss of FDG uptake while other lesions in the same patient failed to respond. Improved overall survival correlated with a decrease in FDG uptake in hepatic lesions (R = -0.929; p = 0.007). CONCLUSIONS: CP-870,893 in combination with gemcitabine was well-tolerated and associated with anti-tumor activity in patients with PDA. Changes in FDG uptake detected on PET/CT imaging provide insight into therapeutic benefit. Phase II studies are warranted.

[25]

TÍTULO / TITLE: - Elevated Preoperative Neutrophil-to-lymphocyte Ratio as a Predictor of Survival After Gastroenterostomy in Patients with Advanced Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Aug 28.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3227-8](#)

AUTORES / AUTHORS: - Sugiura T; Uesaka K; Kanemoto H; Mizuno T; Okamura Y

INSTITUCIÓN / INSTITUTION: - Division of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center, Shizuoka, Japan, t.sugiura@scchr.jp.

RESUMEN / SUMMARY: - BACKGROUND: There is increasing evidence that the presence of an ongoing systemic inflammatory response, especially a high preoperative neutrophil-to-lymphocyte ratio (NLR), is associated with a poor outcome for a variety of common solid tumors. However, few studies have investigated the clinical value of the NLR in patients undergoing gastroenterostomy for advanced pancreatic cancer. METHODS: A total of 83 patients who had symptoms of gastric outlet obstruction due to advanced pancreatic cancer and underwent gastroenterostomy were analyzed. The prognostic significance of the NLR was analyzed. The relationship between the NLR value and postoperative outcome was also evaluated. RESULTS: The median survival time was 9.4 months in patients with an NLR of <4, whereas it was 3.4 months in patients with an NLR of ≥4 (P < 0.001). The multivariate analysis revealed that an

NLR of ≥ 4 , the presence of liver metastases, daily pain, and lack of postoperative chemotherapy were significant prognostic factors. A higher NLR was associated with postoperative morbidity; 13 % of patients with an NLR of < 4 and 36 % of those with an NLR of ≥ 4 ($P = 0.012$) developed morbidities. With regard to quality of life, 96 % of patients with an NLR of < 4 and 36 % of patients with an NLR of ≥ 4 had adequate oral intake of solid food without any support with intravenous nutrition for at least 1 month after surgery ($P < 0.001$). CONCLUSIONS: The preoperative NLR offers important prognostic information for patients who have gastric outlet obstruction due to advanced pancreatic adenocarcinoma.

[26]

TÍTULO / TITLE: - Chronic Hyperinsulinemia Does Not Increase the Production Rate of High-Density Lipoprotein Apolipoprotein AI: Evidence From a Kinetic Study in Patients With Insulinoma.

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

REVISTA / JOURNAL: - Arterioscler Thromb Vasc Biol. 2013 Oct;33(10):2460-5. doi: 10.1161/ATVBAHA.113.301597. Epub 2013 Aug 1.

●● Enlace al texto completo (gratis o de pago) [1161/ATVBAHA.113.301597](#)

AUTORES / AUTHORS: - Duvillard L; Florentin E; Pont F; Petit JM; Baillot-Rudoni S; Penfornis A; Verges B

INSTITUCIÓN / INSTITUTION: - From the Faculte de Medecine, INSERM U866-Universite de Bourgogne, Dijon, France (L.D., E.F., F.P., J.-M.P., B.V.); Laboratoire de Biologie Medicale, CHU, Dijon, France (L.D., E.F.); Service d'Endocrinologie et Maladies Metaboliques, CHU, Dijon, France (J.-M.P. S.B.-R., B.V.); and Service d'Endocrinologie et Maladies Metaboliques, CHU, Besancon, France (A.P.).

RESUMEN / SUMMARY: - OBJECTIVE: In vitro studies showed that insulin stimulates the production of apolipoprotein AI (apoAI). Thus, we hypothesized that chronic hyperinsulinemia could contribute to the increase in the production of high-density lipoprotein apoAI that is observed in metabolic syndrome. APPROACH AND RESULTS: We performed an in vivo kinetic study with stable isotope in 7 patients with insulinoma who showed hyperinsulinemia but no insulin resistance, 8 patients with insulin resistance, and 16 controls. Insulinemia was 3.1x ($P < 0.01$) higher in patients with insulinoma or insulin resistance than in controls in the fasting state and, respectively, 3.5x and 2.6x ($P < 0.05$) higher in the fed state. The high-density lipoprotein apoAI pool size was smaller in patients with insulin resistance than in controls (49.3 ± 5.4 versus 59.6 ± 7.7 mg.kg⁻¹; $P < 0.01$), whereas both the high-density lipoprotein apoAI fractional catabolic rate and the high-density lipoprotein apoAI production rate were higher (0.30 ± 0.07 versus 0.20 ± 0.04 pool.d⁻¹; $P < 0.0001$ and 14.6 ± 1.5 versus 11.5 ± 1.9 mg.kg⁻¹.d⁻¹; $P < 0.01$, respectively). In contrast, no significant difference was observed for these parameters between

patients with insulinoma and controls. In patients with insulinoma, the apoAI pool size tended to be greater than in patients with insulin resistance (56.3+/-8.6 versus 49.3+/-5.4 mg.kg(-1); P=0.078), whereas both the apoAI fractional catabolic rate and the production rate were lower (0.20+/-0.06 versus 0.30+/-0.07 pool.d(-1); P<0.01 and 11.1+/-1.6 versus 14.6+/-1.5 mg.kg(-1).d(-1); P<0.01, respectively). The apoAI fractional catabolic rate was the only variable associated with the apoAI production rate in multivariate analysis and explained 80% of its variance. CONCLUSIONS: Chronic endogenous hyperinsulinemia does not induce any increase in the apoAI production rate, which seems to be more dependent on the apoAI fractional catabolic rate.

[27]

TÍTULO / TITLE: - Proteinase-Activated Receptors Differentially Modulate In Vitro Invasion of Human Pancreatic Adenocarcinoma PANC-1 Cells in Correlation With Changes in the Expression of CDC42 Protein.

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

REVISTA / JOURNAL: - Pancreas. 2013 Aug 5.

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

[1097/MPA.0b013e31829f0b81](#)

AUTORES / AUTHORS: - Segal L; Katz LS; Lupu-Meiri M; Shapira H; Sandbank J; Gershengorn MC; Oron Y

INSTITUCIÓN / INSTITUTION: - From the *Department of Physiology and Pharmacology, Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel; daggerLaboratory of Endocrinology and Receptor Biology, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD; double daggerInstitute of Pathology, Central Lab, Maccabi, Rehovot, Israel; and section signAssaf Harofe Hospital Institute of Pathology and the Department of Pathology, Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel.

RESUMEN / SUMMARY: - OBJECTIVES: Proteinase-activated receptor-1 (PAR-1) and PAR-2 have been associated with increased invasiveness and metastasis in human malignancies. The role of PAR-3 has been less investigated. We examined the role of PARs in a human pancreatic adenocarcinoma PANC-1 cell line phenotype in vitro. METHODS: We knocked down PAR-1, PAR-2, or PAR-3, whereas empty vector-infected cells served as controls. Specific peptide agonists of PARs were used to stimulate the receptors. In vitro assays of colony formation, migration, and invasion were used to characterize the phenotypes, and Western analysis was used to follow cell division control protein 42 homolog (CDC42) expression. RESULTS: PAR-1 and PAR-2 knockdowns (KDs) were markedly less, whereas PAR-3 KDs were robustly more migratory and invasive than the controls. Stimulation of PAR-1 or PAR-2 by their peptide agonists increased, whereas PAR-3 agonist reduced the invasion of the control cells. Knockdowns of all three PARs exhibited changes in the expression of CDC42,

which correlated with the changes in their invasion. Conversely, stimulation of vector-control cells with PAR-1 or PAR-2 agonists enhanced, whereas PAR-3 agonist reduced the expression of CDC42. In the respective KD cells, the effects of the agonists were abrogated. CONCLUSION: The expression and/or activation of PARs is linked to the invasiveness of PANC-1 cells in vitro, probably via modulation of the expression of CDC42.

[28]

TÍTULO / TITLE: - Low Total Lymphocyte Count Is Associated with Poor Survival in Patients with Resected Pancreatic Adenocarcinoma Receiving a GM-CSF Secreting Pancreatic Tumor Vaccine.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Sep 18.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3262-5](#)

AUTORES / AUTHORS: - Schueneman AJ; Sugar EA; Uram J; Bigelow E; Herman JM; Edil BH; Jaffee EM; Zheng L; Laheru DA

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA.

RESUMEN / SUMMARY: - BACKGROUND: Low total lymphocyte count (TLC) and lymphocyte-to-neutrophil ratio have been found to be poor prognostic indicators in several different tumor types at various stages. Although immune-based therapies are under rapid development, it is not known whether baseline complete blood counts, particularly lymphocytes, are associated with the clinical outcomes of patients receiving immunotherapies. METHODS: We performed a retrospective analysis of complete blood count for 59 patients enrolled onto a phase II trial evaluating the integration of an adjuvant immunotherapy-irradiated granulocyte-macrophage colony-stimulating factor (GM-CSF) secreting allogeneic pancreatic tumor vaccine (GVAX)-with standard chemoradiation. RESULTS: After adjusting for nodal status, individuals with a TLC of <1,500 cells/mm³ (10 patients) had significantly higher risk, both in terms of overall survival (OS) [adjusted hazard ratio 2.63, 95 % confidence interval (CI) 1.22-5.67, p = 0.013] and progression-free survival (adjusted hazard ratio 3.07, 95 % CI 1.03-6.93, p = 0.003), compared to those with a TLC of <=1,500 cells/mm³ (49 patients). Adjuvant chemoradiation significantly reduced lymphocyte counts from baseline values. Patients with suppression of their lymphocytes to <500 cells/mm³ after chemoradiation also had shorter disease-free and OS. CONCLUSIONS: Immunosuppressive conditions associated with surgical procedures and chemoradiation may affect the efficacy of immunotherapy.

[29]

TÍTULO / TITLE: - Inhibition of pancreatic carcinoma by homo- and hetero-combinations of antibodies against EGF-receptor and its kin HER2/ErbB-2.

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

REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Sep 17;110(38):15389-94. doi: 10.1073/pnas.1313857110. Epub 2013 Sep 3.

●● Enlace al texto completo (gratis o de pago) [1073/pnas.1313857110](https://doi.org/10.1073/pnas.1313857110)

AUTORES / AUTHORS: - Maron R; Schechter B; Mancini M; Mahlknecht G; Yarden Y; Selam M

INSTITUCIÓN / INSTITUTION: - Departments of Immunology and Biological Regulation, Weizmann Institute of Science, Rehovot 76100, Israel.

RESUMEN / SUMMARY: - Due to intrinsic aggressiveness and lack of effective therapies, prognosis of pancreatic cancer remains dismal. Because the only molecular targeted drug approved for pancreatic ductal adenocarcinoma is a kinase inhibitor specific to the epidermal growth factor receptor (EGFR), and this receptor collaborates with another kinase, called HER2 (human EGF-receptor 2), we assumed that agents targeting EGFR and/or HER2 would effectively retard pancreatic ductal adenocarcinoma. Accordingly, two immunological strategies were tested in animal models: (i) two antibodies able to engage distinct epitopes of either EGFR or HER2 were separately combined, and (ii) pairs of one antibody to EGFR and another to HER2. Unlike the respective single monoclonal antibodies, which induced weak effects, both types of antibody combinations synergized in animals in terms of tumor inhibition. Immunological cooperation may not depend on receptor density, antigenic sites, or the presence of a mutant RAS protein. Nevertheless, both types of antibody combinations enhanced receptor degradation. Future efforts will examine the feasibility of each strategy and the potential of combining them to achieve sustained tumor inhibition.

[30]

TÍTULO / TITLE: - Activated Wnt Signaling in Stroma Contributes to Development of Pancreatic Mucinous Cystic Neoplasms.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Sep 22. pii: S0016-5085(13)01373-5. doi: 10.1053/j.gastro.2013.09.044.

●● Enlace al texto completo (gratis o de pago) [1053/j.gastro.2013.09.044](https://doi.org/10.1053/j.gastro.2013.09.044)

AUTORES / AUTHORS: - Sano M; Driscoll DR; Dejesus-Monge WE; Klimstra DS; Lewis BC

INSTITUCIÓN / INSTITUTION: - Program in Gene Function and Expression, University of Massachusetts Medical School, Worcester, MA, 01605; Division of Pathology, Department of Pathology and Microbiology, Nihon University School of Medicine, Tokyo, 173-8610, Japan. Electronic address: sano.makoto@nihon-u.ac.jp.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Pancreatic mucinous cystic neoplasm (MCN), a cystic tumor of the pancreas that develops most frequently in women, is a potential precursor to pancreatic ductal adenocarcinoma. MCNs develop primarily in the body and tail of the pancreas and are characterized by the presence of a mucinous epithelium and ovarian-like subepithelial stroma. We investigated the involvement of Wnt signaling in KRAS-mediated pancreatic tumorigenesis and development of MCN in mice, and Wnt activation in human MCN samples. METHODS: LSL-KrasG12D, Ptf1a-cre mice were crossed with elastase-tva mice to allow for introduction of genes encoded by the replication-competent avian sarcoma-leukosis virus long-terminal repeat with splice acceptor (RCAS) viruses to pancreatic acinar cells and acinar cell progenitors, post-natally and sporadically. RCAS viruses that expressed Wnt1 were delivered to the pancreatic epithelium of these mice; pancreatic lesions were analyzed by histopathology and immunohistochemical analyses. We analyzed levels of factors in Wnt signaling pathways in 19 MCN samples from patients. RESULTS: Expression of Wnt1 in the pancreatic acinar cells and acinar cell progenitors of female mice led to development of unilocular or multilocular epithelial cysts in the pancreas body and tail, similar to MCN. The cystic lesions resembled the estrogen receptor- and progesterone receptor-positive ovarian-like stroma of MCN, but lacked the typical mucinous epithelium. Activated Wnt signaling, based on nuclear localization of beta-catenin, was detected in the stroma but not cyst epithelium. Wnt signaling to beta-catenin was found to be activated in MCN samples from patients, within the ovarian-like stroma, consistent with the findings in mice. CONCLUSIONS: Based on studies of mice and pancreatic MCN samples from patients, the canonical Wnt signaling pathway becomes activated and promotes development of the ovarian-like stroma to contribute to formation of MCNs.

[31]

TÍTULO / TITLE: - Cachexia in patients with chronic pancreatitis and pancreatic cancer: impact on survival and outcome.

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

REVISTA / JOURNAL: - Nutr Cancer. 2013;65(6):827-33. doi: 10.1080/01635581.2013.804580.

●● Enlace al texto completo (gratis o de pago) [1080/01635581.2013.804580](#)

AUTORES / AUTHORS: - Bachmann J; Buchler MW; Friess H; Martignoni ME

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Klinikum rechts der Isar, Technische Universität München, Munich, Germany. jeannine.bachmann@tum.de

RESUMEN / SUMMARY: - Chronic pancreatitis (CP) and pancreatic adenocarcinoma (PDAC) are the most common diseases of the pancreas. Cachexia-weight loss exceeding 10% of stable body weight-is present in up to 80% of patients with PDAC. Because the mechanisms of cachexia are not well known, this provides a possibility to

compare clinical courses of benign and malignant cachexia. In this study, 382 patients-242 with a PDAC stage UICC II/ 140 with CP-were documented regarding the prevalence of cachexia and its influence on perioperative morbidity and mortality with a special interest to postoperative weight gain and survival. Cachexia was present in 41.4% of CP and 31% of cancer patients. We could demonstrate more pronounced systemic effects of cachexia in patients with PDAC. Weight loss was faster in PDAC patients, the amount of weight loss did not differ significantly between the groups. Cachexia had a significant impact on survival and the postoperative course in patients with PDAC and tumor resection. The development of cachexia is faster in patients with a malignant disease and the systemic effects are more pronounced. Therefore, tumor cachexia should be considered as a different entity than cachexia in benign diseases.

[32]

TÍTULO / TITLE: - Sox9-Dependent Acinar-to-Ductal Reprogramming is Critical for Pancreatic Intraepithelial Neoplasia Formation.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Oct;145(4):904-7. doi: 10.1053/j.gastro.2013.08.028. Epub 2013 Aug 21.

●● Enlace al texto completo (gratis o de pago) [1053/j.gastro.2013.08.028](#)

AUTORES / AUTHORS: - Fukuda A; Chiba T

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology and Hepatology, Graduate School of Medicine, Kyoto University, Kyoto, Japan.

[33]

TÍTULO / TITLE: - Identification and Manipulation of Biliary Metaplasia in Pancreatic Tumors.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Aug 30. pii: S0016-5085(13)01273-0. doi: 10.1053/j.gastro.2013.08.053.

●● Enlace al texto completo (gratis o de pago) [1053/j.gastro.2013.08.053](#)

AUTORES / AUTHORS: - Delgiorno KE; Hall JC; Takeuchi KK; Pan FC; Halbrook CJ; Washington MK; Olive KP; Spence J; Sipos B; Wright CV; Wells JM; Crawford HC

INSTITUCIÓN / INSTITUTION: - Department of Molecular Genetics and Microbiology, Stony Brook University, Stony Brook University, Stony Brook, NY 11794; Department of Cancer Biology, Mayo Clinic, Jacksonville, FL 32224.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Metaplasias often have characteristics of developmentally related tissues. Pancreatic metaplastic ducts are usually associated with pancreatitis and pancreatic ductal adenocarcinoma. The tuft cell is a chemosensory cell that responds to signals in the extracellular environment via

effector molecules. Commonly found in the biliary tract, tuft cells are absent from normal murine pancreas. Using the aberrant appearance of tuft cells as an indicator, we tested if pancreatic metaplasia represents transdifferentiation to a biliary phenotype and what effect this has on pancreatic tumorigenesis. METHODS: We analyzed pancreatic tissue and tumors that developed in mice that express an activated form of Kras (KrasLSL-G12D/+;Ptf1aCre/+ mice). Normal bile duct, pancreatic duct, and tumor-associated metaplasias from the mice were analyzed for tuft cell and biliary progenitor markers, including SOX17, a transcription factor that regulates biliary development. We also analyzed pancreatic tissues from mice expressing transgenic SOX17 alone (ROSA^{Ta}/+;Ptf1aCreERTM/+;tetO-SOX17) or along with activated Kras (ROSA^{Ta}/+;Ptf1aCreERTM/+;tetO-SOX17;KrasLSL-G12D/+). RESULTS: Tuft cells were frequently found in areas of pancreatic metaplasia, decreased throughout tumor progression, and were absent from invasive tumors. Analysis of the pancreatobiliary ductal systems of mice revealed tuft cells in the biliary tract, but not the normal pancreatic duct. Analysis for biliary markers revealed expression of SOX17 in pancreatic metaplasia and tumors. Pancreas-specific overexpression of SOX17 led to ductal metaplasia along with inflammation and collagen deposition. Mice that overexpressed SOX17 along with KrasG12D had a greater degree of transformed tissue compared with mice expressing only KrasG12D. Immunofluorescence analysis of human pancreatic tissue arrays revealed the presence of tuft cells in metaplasia and early-stage tumors, along with SOX17 expression, consistent with a biliary phenotype. CONCLUSIONS: Expression of KrasG12D and SOX17 in mice induces development of metaplasias with a biliary phenotype, containing tuft cells. Tuft cells express a number of tumorigenic factors that can alter the microenvironment. Expression of SOX17 induces pancreatitis and promotes KrasG12D-induced tumorigenesis in mice.

[34]

TÍTULO / TITLE: - Evaluation of ipilimumab in combination with allogeneic pancreatic tumor cells transfected with a GM-CSF gene in previously treated pancreatic cancer.

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

REVISTA / JOURNAL: - J Immunother. 2013 Sep;36(7):382-9. doi: 10.1097/CJI.0b013e31829fb7a2.

●● Enlace al texto completo (gratis o de pago) [1097/CJI.0b013e31829fb7a2](#)

AUTORES / AUTHORS: - Le DT; Lutz E; Uram JN; Sugar EA; Onners B; Solt S; Zheng L; Diaz LA Jr; Donehower RC; Jaffee EM; Laheru DA

INSTITUCIÓN / INSTITUTION: - The Sidney Kimmel Cancer Center, the Skip Viragh Center for Pancreatic Cancer, Research and Clinical Care, and the Sol Goldman Pancreatic Cancer Center at Johns Hopkins, Baltimore, MD, USA. dle2@jhmi.edu

RESUMEN / SUMMARY: - Preclinical reports support the concept of synergy between cancer vaccines and immune checkpoint blockade in nonimmunogenic tumors. In

particular, cytotoxic T lymphocyte-associated antigen-4 (CTLA-4) antibodies have been successfully combined with GM-CSF cell-based vaccines (GVAX). Ipilimumab (anti-CTLA-4) has been tested as a single agent in patients with pancreatic ductal adenocarcinoma (PDA) resulting in a delayed response at a dose of 3 mg/kg. Our study evaluated ipilimumab 10 mg/kg (arm 1) and ipilimumab 10 mg/kg + GVAX (arm 2). A total of 30 patients with previously treated advanced PDA were randomized (1:1). Induction doses were administered every 3 weeks for a total of 4 doses followed by maintenance dosing every 12 weeks. Two patients in arm 1 showed evidence of stable disease (7 and 22 wk) but none demonstrated CA19-9 biochemical responses. In contrast, 3 patients in arm 2 had evidence of prolonged disease stabilization (31, 71, and 81 wk) and 7 patients experienced CA19-9 declines. In 2 of these patients, disease stabilization occurred after an initial period of progression. The median overall survival (OS) (3.6 vs. 5.7 mo, hazards ratio: 0.51, P = 0.072) and 1 year OS (7 vs. 27%) favored arm 2. Similar to prior ipilimumab studies, 20% of patients in each arm had grade 3/4 immune-related adverse events. Among patients with OS > 4.3 months, there was an increase in the peak mesothelin-specific T cells (P = 0.014) and enhancement of the T-cell repertoire (P = 0.031). In conclusion, checkpoint blockade in combination with GVAX has the potential for clinical benefit and should be evaluated in a larger study.

[35]

TÍTULO / TITLE: - Reponse to Comments on: Butler et al. Marked Expansion of Exocrine and Endocrine Pancreas With Incretin Therapy in Humans With Increased Exocrine Pancreas Dysplasia and the Potential for Glucagon-Producing Neuroendocrine Tumors. Diabetes 2013;62:2595-2604.

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

REVISTA / JOURNAL: - Diabetes. 2013 Oct;62(10):e19-22. doi: 10.2337/db13-0996.

●● [Enlace al texto completo \(gratis o de pago\) 2337/db13-0996](#)

AUTORES / AUTHORS: - Butler AE; Campbell-Thompson M; Gurlo T; Dawson DW; Atkinson M; Butler PC

INSTITUCIÓN / INSTITUTION: - Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California.

[36]

TÍTULO / TITLE: - Comment on: Butler et al. Marked Expansion of Exocrine and Endocrine Pancreas With Incretin Therapy in Humans With Increased Exocrine Pancreas Dysplasia and the Potential for Glucagon-Producing Neuroendocrine Tumors. Diabetes 2013;62:2595-2604.

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

REVISTA / JOURNAL: - Diabetes. 2013 Oct;62(10):e18. doi: 10.2337/db13-0525.

●● Enlace al texto completo (gratis o de pago) [2337/db13-0525](#)

AUTORES / AUTHORS: - Engel SS; Golm GT; Luring B

INSTITUCIÓN / INSTITUTION: - Merck Sharp & Dohme Corp., Whitehouse Station, New Jersey.

[37]

TÍTULO / TITLE: - Comment on: Butler et al. Marked Expansion of Exocrine and Endocrine Pancreas With Incretin Therapy in Humans With Increased Exocrine Pancreas Dysplasia and the Potential for Glucagon-Producing Neuroendocrine Tumors. Diabetes 2013;62:2595-2604.

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

REVISTA / JOURNAL: - Diabetes. 2013 Oct;62(10):e16-7. doi: 10.2337/db13-0690.

●● Enlace al texto completo (gratis o de pago) [2337/db13-0690](#)

AUTORES / AUTHORS: - Heine RJ; Fu H; Kendall DM; Moller DE

INSTITUCIÓN / INSTITUTION: - Lilly Research Laboratories and Lilly Diabetes, Eli Lilly & Co., Indianapolis, Indiana.

[38]

TÍTULO / TITLE: - Targeting of NAD metabolism in pancreatic cancer cells: potential novel therapy for pancreatic tumors.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Sep 11.

●● Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-13-0150](#)

AUTORES / AUTHORS: - Chini CC; Gonzalez Guerrico A; Nin V; Camacho-Pereira J; Escande C; Barbosa M; Chini EN

INSTITUCIÓN / INSTITUTION: - Aging Center, Mayo Clinic.

RESUMEN / SUMMARY: - PURPOSE: Here, we describe a novel interplay between NAD synthesis and degradation involved in pancreatic tumor growth. EXPERIMENTAL DESIGN: We used human pancreatic cancer cells both in vitro (cell culture experiments) and in vivo (xenograft experiments) to demonstrate the role of NAD synthesis and degradation in tumor cell metabolism and growth. RESULTS: We demonstrated that pharmacological and genetic targeting of Nampt, the key enzyme in the NAD salvage synthesis pathway, inhibits cell growth and survival of pancreatic cancer cells. These changes were accompanied by a reduction of NAD levels, glycolytic flux, lactate production, mitochondrial function, and levels of ATP. The massive reduction in overall metabolic activity induced by Nampt inhibition was accompanied by a dramatic decrease in pancreatic tumor growth. The results of the mechanistic experiments showed that neither the NAD-dependent enzymes PARP-1, nor SIRT1 play a significant role on the effect of Nampt inhibition on pancreatic cancer cells. However,

we identified a role for the NAD degradation pathway mediated by the NADase CD38 on the sensitivity to Nampt inhibition. The responsiveness to Nampt inhibition is modulated by the expression of CD38; low levels of this enzyme decrease the sensitivity to Nampt inhibition. In contrast, its overexpression decreased cell growth in vitro and in vivo and further increases the sensitivity to Nampt inhibition.

CONCLUSIONS: Our study demonstrates that NAD metabolism is essential for pancreatic cancer cell survival and proliferation and that targeting NAD synthesis via the Nampt pathway could lead to novel therapeutic treatments for pancreatic cancer.

[39]

TÍTULO / TITLE: - Stereotactic Radiosurgery Plays a Critical Role in Enhancing Long-term Survival in a Patient with Pancreatic Cancer Metastatic to the Brain.

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

REVISTA / JOURNAL: - Anticancer Res. 2013 Sep;33(9):3899-903.

AUTORES / AUTHORS: - Rajappa P; Margetis K; Wernicke G; Ginter P; Cope W; Sherr DL; Lavi E; Fine RL; Schwartz TH; Bruckner H; Pannullo SC

INSTITUCIÓN / INSTITUTION: - Weill Cornell Brain and Spine Center, 525 East 69th Street Starr Pavilion, 651, New York, NY 10065, box 99, U.S.A. scp2002@med.cornell.edu.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is an aggressive disease which metastasizes readily. The presence of brain metastases from pancreatic cancer is rare and it carries a poor prognosis. Our approach to treating these lesions stresses extensive use of stereotactic radiosurgery (SRS), whereas other reports focus on surgical resection. Case Report: Information regarding the patient's clinical history was extracted from a retrospective review of the medical records and imaging studies. The patient survived seven years after his primary diagnosis of pancreatic cancer, and 36 months after diagnosis of metastatic disease to the brain. In addition to surgical resection and the use of multiple chemotherapeutic agents, the patient received six separate radiosurgery treatments. CONCLUSION: We present a case of brain metastasis from pancreatic cancer that is remarkable for an unusually long survivorship and discuss the utility of SRS along with a multimodality treatment approach for dealing with these cases.

[40]

TÍTULO / TITLE: - Does long-term survival in patients with pancreatic cancer really exist?- Results from the CONKO-001 study.

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

REVISTA / JOURNAL: - J Surg Oncol. 2013 Aug 23. doi: 10.1002/jso.23409.

●● Enlace al texto completo (gratis o de pago) 1002/jso.23409

AUTORES / AUTHORS: - Sinn M; Striefler JK; Sinn BV; Sallmon D; Bischoff S; Stieler JM; Pelzer U; Bahra M; Neuhaus P; Dorken B; Denkert C; Riess H; Oettle H

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology and Haematology, Charite-Universitätsmedizin Berlin, Germany.

RESUMEN / SUMMARY: - BACKGROUND: Long-term survival (LTS) in patients (pts) with pancreatic cancer is still uncommon, little data is available to identify long-term survivors. The CONKO-001 study, which established gemcitabine after resection as adjuvant therapy, may provide data to answer this question. METHODS: CONKO-001 pts with an overall survival ≥ 5 years were compared to those who survived < 5 years. Central re-evaluation of primary histology was performed. Univariate analysis with the chi² -test identified qualifying factors. Logistic regression was used to investigate the influence of these covariates on LTS. RESULTS: Of the evaluable 354 CONKO-001 pts, 54 (15%) with an overall survival ≥ 5 years were identified. It was possible to obtain tumor specimens of 39 pts (72%). Histological re-evaluation confirmed adenocarcinoma in 38 pts, 1 showed a high-grade neuroendocrine tumor. Univariate analysis for all 53 LTS pts with adenocarcinoma compared to the remaining 300 non-LTS pts revealed as relevant active treatment, tumor grading, tumor size, lymph nodes. No significance could be demonstrated for resection margin, sex, age, Karnofsky performance status, CA 19-9 at study entry. In multivariate analysis, tumor grading, active treatment, tumor size, lymph node involvement were independent prognostic factors for LTS. CONCLUSION: Long-term survival can be achieved in adenocarcinoma of the pancreas. J. Surg. Oncol. 2013 9999:1-5. © 2013 Wiley Periodicals, Inc.

[41]

TÍTULO / TITLE: - Generation of CTL responses against pancreatic cancer in vitro using dendritic cells co-transfected with MUC4 and survivin RNA.

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

REVISTA / JOURNAL: - Vaccine. 2013 Sep 23;31(41):4585-90. doi: 10.1016/j.vaccine.2013.07.055. Epub 2013 Aug 6.

●● Enlace al texto completo (gratis o de pago) [1016/j.vaccine.2013.07.055](http://dx.doi.org/10.1016/j.vaccine.2013.07.055)

AUTORES / AUTHORS: - Chen J; Guo XZ; Li HY; Liu X; Ren LN; Wang D; Zhao JJ

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, The Shenyang General Hospital of PLA, No. 83 Wenhua Road, Shenyang City, Liaoning, China.

RESUMEN / SUMMARY: - Pancreatic cancer (PC) is one of the most devastating human malignancies without effective therapies. Tumor vaccine based on RNA-transfected dendritic cells (DCs) has emerged as an alternative therapeutic approach for a variety of human cancers including advanced PC. In the present study we compared the cytotoxic T lymphocyte (CTL) responses against PC cells in vitro, which were induced by DCs co-transfected with two mRNAs of tumor associated-antigens (TAA) MUC4 and

survivin, versus DCs transfected with a single mRNA encoding either MUC4 or survivin. DCs co-transfected with two TAA mRNAs were found to induce stronger CTL responses against PC target cells in vitro, compared with the DCs transfected with a single mRNA. Moreover, the antigen-specific CTL responses were MHC class I-restricted. These results provide an experimental foundation for further clinical investigations of DC vaccines encoding multiple TAA epitopes for metastatic PC.

[42]

TÍTULO / TITLE: - Optimal control of nausea and vomiting with a three-drug antiemetic regimen with aprepitant in metastatic pancreatic cancer patients treated with first-line modified FOLFIRINOX.

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

REVISTA / JOURNAL: - Support Care Cancer. 2013 Nov;21(11):2955-2956. Epub 2013 Aug 23.

●● Enlace al texto completo (gratis o de pago) [1007/s00520-013-1944-y](#)

AUTORES / AUTHORS: - Silvestris N; Brunetti AE; Russano M; Nardulli P

INSTITUCIÓN / INSTITUTION: - Medical Oncology Unit, National Cancer Institute "Giovanni Paolo II", Viale Orazio Flacco, 65, 70124, Bari, Italy, n.silvestris@oncologico.bari.it.

[43]

TÍTULO / TITLE: - Phase II Study on Combined Intravenous and Intra-Arterial Chemotherapy with Gemcitabine and Mitomycin C in Patients with Advanced Pancreatic Cancer.

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

REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Aug;60(126):1492-6. doi: 10.5754/hge11805.

●● Enlace al texto completo (gratis o de pago) [5754/hge11805](#)

AUTORES / AUTHORS: - Heinrich S; Kraft D; Staib-Sebler E; Schwarz W; Gog C; Vogl T; Lorenz M

RESUMEN / SUMMARY: - :Background/Aims: This prospective phase II study on a combination of intraarterial (i.a.) and systemic chemotherapy was performed to test whether regional chemotherapy may overcome the chemoresistance of pancreatic cancer. Methodology: One treatment cycle consisted of an i.a. infusion through an angiographic catheter into the celiac artery of 8.5mg/m² mitomycin C (MMC) and 500 mg/m² gemcitabine on days 1 and 22, and intravenous infusions of 500 mg/m² gemcitabine on days 8 and 15. Study-endpoints were overall survival and tumor response as measured by computed tomography (CT). Treatment was continued until disease progression or complete remission on CT. Results: Thirty-seven treatment cycles were performed in 17 patients. The most frequent side effects were

hematological with 18 episodes of grade III/IV toxicities. According to radiographic and tumor marker criteria, four (24%) and seven patients (41%), respectively, demonstrated an objective response. The median actual progression-free and overall survivals were 4.6 and 9.1 months, respectively. Patients without distant metastases had a longer median survival (15 months) than those with distant metastases (7.1 months, $p = 0.037$). Conclusions: This combination treatment was well tolerated and resulted in tumor response rates, median overall- and progression-free survival times superior to systemic gemcitabine chemotherapy, and comparable to the more toxic FOLFIRINOX regimen.

[44]

TÍTULO / TITLE: - Does an aberrant right hepatic artery really influence the short- and long-term results of a pancreaticoduodenectomy for malignant disease? A matched case-controlled study.

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

REVISTA / JOURNAL: - J Surg Res. 2013 Jul 26. pii: S0022-4804(13)00701-4. doi: 10.1016/j.jss.2013.07.015.

●● Enlace al texto completo (gratis o de pago) [1016/j.jss.2013.07.015](#)

AUTORES / AUTHORS: - Sulpice L; Rayar M; Paquet C; Bergeat D; Merdrignac A; Cunin D; Meunier B; Boudjema K

INSTITUCIÓN / INSTITUTION: - Service de Chirurgie Hepatobiliaire et Digestive, Hopital Pontchaillou, Centre Hospitalier Universitaire, Universite de Rennes 1, Rennes, France; Inserm, UMR991, Foie, Metabolismes et Cancer, Universite de Rennes 1, Rennes, France. Electronic address: laurent.sulpice@chu-rennes.fr.

RESUMEN / SUMMARY: - BACKGROUND: An aberrant right hepatic artery (ARHA) is a common anatomic variation. The risk associated with ARHA during pancreaticoduodenectomy (PD) continues to be debated. The aim of this study was to compare the clinical outcomes and survival after PD with ARHA against a matched cohort of patients without ARHA. METHODS: PD with an ARHA performed between January 2000 and September 2009 were retrospectively analyzed. Patients with an ARHA (group 1) were matched (1:2) to patients without an ARHA (group 2) according to gender, age, body mass index, type of tumor, and lymph node status. Peri- and postoperative outcomes were compared between the two groups. Overall survival and disease-free survival were estimated by Kaplan-Meier method and compared with log-rank test. RESULTS: A total of 29 patients (group 1) and 55 patients (group 2) were compared. In group 1, an ARHA entered the tumor in six cases (20.7%), was sacrificed in four cases, and repaired in two cases. There was no difference regarding the rate of intraoperative and postoperative variables between the two groups. The oncological clearance ($P = 0.731$) and survival (overall survival, $P = 0.843$; disease-free survival, $P =$

0.832) were also similar. CONCLUSIONS: Our study showed that the presence of an ARHA during PD was not associated with worse postoperative outcomes or survival.

[45]

TÍTULO / TITLE: - A retrospective study of S-1 and oxaliplatin combination chemotherapy in patients with refractory pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Sep 1.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2278-7](#)

AUTORES / AUTHORS: - Takahara N; Isayama H; Nakai Y; Sasaki T; Hamada T; Uchino R; Mizuno S; Miyabayashi K; Kogure H; Yamamoto N; Sasahira 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: The aim of this study was to evaluate S-1 and oxaliplatin combination chemotherapy (SOX) in patients with refractory pancreatic cancer (PC). METHODS: Consecutive patients with advanced PC refractory to gemcitabine who were treated with oral S-1 (80 mg/m²) on days 1-14 and intravenous oxaliplatin (100 mg/m²) on day 1 every 3 weeks were studied retrospectively. The primary end point was the objective response rate (ORR). The secondary end points were progression-free survival (PFS), overall survival (OS), the disease control rate (DCR), and safety. RESULTS: Between March 2009 and October 2011, 30 patients were treated with SOX, with a median of two courses (range 1-8). The ORR and DCR were 10.0 and 50.0 %, respectively. Median PFS and OS were 3.4 months (95 % confidence interval [CI] 1.3-5.3) and 5.0 months (95 % CI 3.4-7.4), respectively. The median PFS and OS were 5.6 and 9.1 months in patients receiving S-1 and oxaliplatin as a second-line treatment. Major grade 3 or 4 adverse events included neutropenia (10.0 %), anemia (3.3 %), and diarrhea (6.7 %). CONCLUSIONS: SOX was well tolerated and moderately effective in patients with refractory PC.

[46]

TÍTULO / TITLE: - Identifying patients with undetected pancreatic cancer in primary care: an independent and external validation of Q Cancer(®) (Pancreas).

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

REVISTA / JOURNAL: - Br J Gen Pract. 2013 Sep;63(614):636-42. doi: 10.3399/bjgp13X671623.

●● Enlace al texto completo (gratis o de pago) [3399/bjgp13X671623](#)

AUTORES / AUTHORS: - Collins GS; Altman DG

INSTITUCIÓN / INSTITUTION: - Centre for Statistics in Medicine, Oxford, UK.

RESUMEN / SUMMARY: - BACKGROUND: Despite its rarity, the prognosis of pancreatic cancer is very poor and it is a major cause of cancer mortality; being ranked fourth in the world, it has one of the worst survival rates of any cancer. AIM: To evaluate the performance of QCancer[®] (Pancreas) for predicting the absolute risk of pancreatic cancer in an independent UK cohort of patients, from general practice records. DESIGN AND SETTING: Prospective cohort study to evaluate the performance QCancer (Pancreas) prediction models in 364 practices from the UK, contributing to The Health Improvement Network (THIN) database. METHOD: Records were extracted from the THIN database for 2.15 million patients registered with a general practice surgery between 1 January 2000 and 30 June 2008, aged 30-84 years (3.74 million person-years), with 618 pancreatic cancer cases. Pancreatic cancer was defined as incident diagnosis of pancreatic cancer during the 2 years after study entry. RESULTS: The results from this independent and external validation of QCancer (Pancreas) demonstrated good performance data on a large cohort of general practice patients. QCancer (Pancreas) had very good discrimination properties, with areas under the receiver operating characteristic curve of 0.89 and 0.92 for females and males respectively. QCancer (Pancreas) explained 60% and 67% of the variation in females and males respectively. QCancer (Pancreas) over-predicted risk in both females and males, notably in older patients. CONCLUSION: QCancer (Pancreas) is potentially useful for identifying undetected cases of pancreatic cancer in primary care in the UK.

[47]

TÍTULO / TITLE: - Clinicopathologic characteristics of pancreatic neuroendocrine tumors and relation of somatostatin receptor type 2^a to outcomes.

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

REVISTA / JOURNAL: - Cancer. 2013 Sep 10. doi: 10.1002/cncr.28341.

●● [Enlace al texto completo \(gratis o de pago\) 1002/cncr.28341](#)

AUTORES / AUTHORS: - Okuwaki K; Kida M; Mikami T; Yamauchi H; Imaizumi H; Miyazawa S; Iwai T; Takezawa M; Saegusa M; Watanabe M; Koizumi W

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Kitasato University East Hospital, Kanagawa, Japan.

RESUMEN / SUMMARY: - BACKGROUND: The impact of somatostatin receptor type 2 (SSTR-2^a) expression levels on outcomes in patients with pancreatic neuroendocrine tumors (PNETs) has not been evaluated. METHODS: Correlations between clinicopathologic characteristics, including SSTR-2^a expression and outcomes, were retrospectively studied in 79 patients with pancreatic neuroendocrine tumors (PNETs). RESULTS: The SSTR-2^a score was 0 in 27% of patients, 1 in 24% of patients, 3 in 30% of patients, and 4 in 18% of patients. The overall survival rate was 87% at 1 year, 77% at 3 years, and 71% at 5 years. On univariate analysis, a pancreatic tumor that measured ≥ 20 mm in greatest dimension, stage IV disease, vascular invasion, neuroendocrine

carcinoma (NEC), and an SSTR-2^a score of 0 were associated significantly with poor outcomes. On multivariate analysis, NEC (P = .000; hazard ratio, 28.8; 95% confidence interval, 7.502-111.240) and an SSTR-2^a score of 0 (P = .001; hazard ratio, 3.611; 95% confidence interval, 1.344-9.702) were related independently to poor outcomes. CONCLUSIONS: The current analysis of prognostic factors in patients with PNETs demonstrated that NEC and an SSTR-2^a score of 0 both were significant independent predictors of poor outcomes. The results suggest that the assessment of SSTR-2^a may facilitate the selection of treatment regimens and the prediction of outcomes. Because a considerable proportion of patients with NEC have SSTR-2^a-positive tumors, further analyses of the usefulness of somatostatin analogues are warranted in patients who have SSTR-2^a-positive NEC. Cancer 2013. © 2013 American Cancer Society.

[48]

TÍTULO / TITLE: - Reduced expression of bone morphogenetic protein receptor IA in pancreatic cancer is associated with a poor prognosis.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Oct 1;109(7):1805-1812. doi: 10.1038/bjc.2013.486. Epub 2013 Aug 22.

●● Enlace al texto completo (gratis o de pago) [1038/bjc.2013.486](#)

AUTORES / AUTHORS: - Voorneveld PW; Stache V; Jacobs RJ; Smolders E; Sitters AI; Liesker A; S Korkmaz K; Lam SM; De Miranda NF; Morreau H; Kodach LL; Hardwick JC
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands.

RESUMEN / SUMMARY: - Background: The expression of SMAD4, the central component of the transforming growth factor-beta (TGF-beta) and bone morphogenetic protein (BMP) signalling pathways, is lost in 50% of pancreatic cancers and is associated with a poor survival. Although the TGF-beta pathway has been extensively studied and characterised in pancreatic cancer, there is very limited data on BMP signalling, a well-known tumour-suppressor pathway. BMP signalling can be lost not only at the level of SMAD4 but also at the level of BMP receptors (BMPRs), as has been described in colorectal cancer. Methods: We performed immunohistochemical analysis of the expression levels of BMP signalling components in pancreatic cancer and correlated these with survival. We also manipulated the activity of BMP signalling in vitro. Results: Reduced expression of BMPRIA is associated with a significantly worse survival, primarily in a subset of SMAD4-positive cancers. In vitro inactivation of SMAD4-dependent BMP signalling increases proliferation and invasion of pancreatic cancer cells, whereas inactivation of BMP signalling in SMAD4-negative cells does not change the proliferation and invasion or leads to an opposite effect. Conclusion: Our data suggest that BMPRIA expression is a good prognostic marker and that the BMP pathway is a potential target for future therapeutic interventions in pancreatic cancer.

[49]

TÍTULO / TITLE: - Treatment Strategy for Main Duct Intraductal Papillary Mucinous Neoplasms of the Pancreas Based on the Assessment of Recurrence in the Remnant Pancreas After Resection: A Retrospective Review.

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

REVISTA / JOURNAL: - Ann Surg. 2013 Sep 6.

●● Enlace al texto completo (gratis o de pago) [1097/SLA.0b013e3182a690ff](#)

AUTORES / AUTHORS: - Tamura K; Ohtsuka T; Ideno N; Aso T; Shindo K; Aishima S; Ohuchida K; Takahata S; Ushijima Y; Ito T; Oda Y; Mizumoto K; Tanaka M

INSTITUCIÓN / INSTITUTION: - Departments of *Surgery and Oncology daggerAnatomic Pathology double daggerClinical Radiology, and section signMedicine and Bioregulatory Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.

RESUMEN / SUMMARY: - **OBJECTIVES::** To clarify the recurrence pattern after resection of main duct intraductal papillary mucinous neoplasms (MD-IPMNs) using molecular analyses and determine the most adequate treatment strategy. **BACKGROUND::** The most appropriate resection line for MD-IPMNs remains an unresolved issue. **METHODS::** Medical records of 56 patients with pancreatectomy were retrospectively reviewed. Histological subtypes and Kras/GNAS mutations were assessed in patients with recurrence in the remnant pancreas. **RESULTS::** Forty-nine patients underwent partial pancreatectomy and 7 underwent total pancreatectomy. Thirty-six patients (64%) had malignant MD-IPMNs. Recurrence was observed in 7 of 49 patients (14%), including 6 with malignant IPMNs and 1 with pancreatic ductal adenocarcinoma, all of whom underwent remnant pancreatectomy. The cumulative disease-specific survival rate of patients with pancreatic recurrence was greater than that of patients with extrapancreatic recurrence ($P < 0.001$). Although the pancreatic margin status at the initial operation did not affect the pancreatic recurrence rate, all 4 recurrent IPMNs examined had histological subtypes and Kras/GNAS mutations identical to those of the initial lesions. Four patients experienced recurrence in the remnant pancreas or systemic recurrence after resection of high-grade dysplasia of MD-IPMN. Three of the 56 patients had concomitant pancreatic ductal adenocarcinomas and MD-IPMNs. **CONCLUSIONS::** One-step total pancreatectomy can be avoided, and remnant total pancreatectomy would lead to favorable outcomes even in patients with pancreatic recurrence, some cases of which seem to involve residual lesions. Postoperative surveillance of high-grade dysplasia should be performed as if malignant, and close attention should be paid to the occurrence of concomitant pancreatic ductal adenocarcinomas in patients with MD-IPMNs.

[50]

TÍTULO / TITLE: - Carboxyl-ester lipase Maturity-Onset Diabetes of the Young is Associated with Development of Pancreatic Cysts and Upregulated MAPK Signaling in Secretin-stimulated duodenal fluid.

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

REVISTA / JOURNAL: - Diabetes. 2013 Sep 23.

●● Enlace al texto completo (gratis o de pago) [2337/db13-1012](#)

AUTORES / AUTHORS: - Raeder H; McAllister FE; Tjora E; Bhatt S; Haldorsen I; Hu J; Willems SM; Vesterhus M; El Ouaamari A; Liu M; Raeder MB; Immervoll H; Hoem D; Dimcevski G; Njolstad PR; Molven A; Gygi SP; Kulkarni RN

INSTITUCIÓN / INSTITUTION: - Section of Islet Cell Biology and Regenerative Medicine, Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA.

RESUMEN / SUMMARY: - CEL-MODY is a monogenic form of diabetes and pancreatic exocrine dysfunction due to mutations in the carboxyl-ester lipase gene CEL. The pathogenic mechanism for diabetes development is unknown. Since CEL is expressed mainly in pancreatic acinar cells, we asked whether we could find structural pancreatic changes in CEL-MODY subjects during the course of diabetes development.

Furthermore, we hypothesized that the diseased pancreas releases proteins which are detectable in pancreatic fluid and potentially reflected activation or inactivation of disease-specific pathways. We therefore investigated non-diabetic and diabetic CEL mutation carriers by pancreatic imaging studies and secretin-stimulated duodenal juice sampling. The secretin-stimulated duodenal juice was studied using cytokine assays, triple-stage mass spectrometry (MS3) and multiplexed mass spectrometry-based measurement of kinase activities. We identified multiple pancreatic cysts in all the eight diabetic mutation carriers but not in any of the four non-diabetic mutation carriers or the six healthy controls. Furthermore, we identified upregulated MAPK target proteins and MAPK-driven cytokines and increased MAPK activity in the secretin-stimulated duodenal juice. These findings show that subjects with CEL-MODY develop multiple pancreatic cysts by the time they develop diabetes and that upregulated MAPK signaling in the pancreatic secretome may reflect the pathophysiological development of pancreatic cysts and diabetes.

[51]

TÍTULO / TITLE: - Interaction of Polymorphisms in Mitotic Regulator Genes With Cigarette Smoking and Pancreatic Cancer Risk.

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

REVISTA / JOURNAL: - Mol Carcinog. 2013 Jun 12. doi: 10.1002/mc.22037.

●● Enlace al texto completo (gratis o de pago) [1002/mc.22037](#)

AUTORES / AUTHORS: - Jang JH; Cotterchio M; Borgida A; Liu G; Gallinger S; Cleary SP

INSTITUCIÓN / INSTITUTION: - Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; Prevention and Cancer Control, Cancer Care Ontario, Toronto, Ontario, Canada.

RESUMEN / SUMMARY: - Mitotic regulator genes have been associated with several cancers, however little is known about their possible association with pancreatic cancer. Smoking and family history are the strongest risk factors for this highly fatal disease. The main purpose of this study was to determine if polymorphisms of mitotic regulator genes are associated with pancreatic cancer and whether they modify the association between cigarette smoking and pancreatic cancer risk. A population-based case-control study was conducted in Ontario with 455 pathology-confirmed pancreatic cancer cases and 893 controls. Cigarette smoking history was collected using questionnaires and DNA obtained from blood samples. Genotypes were determined by mass-spectrometry. Odds ratio estimates were obtained using multivariate logistic regression. Interactions between genetic variant and smoking were assessed using stratified analyses and the likelihood ratio statistic (significance $P < 0.05$). Variants of MCPH1, FYN, APC, PRKCA, NIN, TopBP1, RIPK1, and SNW1 were not independently associated with pancreatic cancer risk. A significant interaction was observed between pack-years and MCPH1-2550-C > T ($P = 0.02$). Compared to never smokers, individuals with 10-27 pack-years and MCPH1-2550-CC genotype were at increased risk for pancreatic cancer (MVOR = 2.49, 95% confidence interval [95% CI]: 1.55, 4.00) as were those with >27 pack-years and MCPH1-2550-TC genotype (MVOR = 2.42, 95% CI: 1.45, 4.05). A significant interaction was observed between smoking status and TopBP1-3257-A > G ($P = 0.04$) using a dominant model. Current smokers with the TopBP1-3257 A allele were at increased risk for pancreatic cancer (MVOR = 2.55, 95% CI: 1.77, 3.67). MCPH1-2550-C > T and TopBP1-3257-A > G modify the association between smoking and pancreatic cancer. These findings provide insights into the potential molecular mechanisms behind smoking-associated pancreatic cancer. © 2013 Wiley Periodicals, Inc.

[52]

TÍTULO / TITLE: - Race Does Not Impact Pancreatic Cancer Treatment and Survival in an Equal Access Federal Health Care System.

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

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

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3130-3](#)

AUTORES / AUTHORS: - Lee S; Reha JL; Tzeng CW; Massarweh NN; Chang GJ; Hetz SP; Fleming JB; Lee JE; Katz MH

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

RESUMEN / SUMMARY: - BACKGROUND: Black patients with pancreatic adenocarcinoma (PDAC) have been reported to undergo surgical resection less frequently and to have a shorter overall survival duration than white patients. We sought to determine whether disparities in clinical management and overall survival exist between black and white patients with PDAC treated in an equal access health care system. METHODS: Using the Department of Defense (DoD) tumor registry database from 1993 to 2007, patient, tumor, and treatment factors were analyzed to compare rates of therapy and survival between black and white patients. RESULTS: Of 1,008 patients with PDAC, 157 were black (15 %). Thirty-six percent of black and 37 % of white patients presented with locoregional disease ($p = 0.85$). Among those with locoregional cancers, the odds of black patients having received surgical resection (odds ratio [OR] 1.06, 95 % confidence interval [CI] 0.60-1.89), chemotherapy (OR 0.92, 95 % CI 0.49-1.73) and radiotherapy (OR 1.14, 95 % CI 0.61-2.10) were not different from those of whites. Among those with distant disease, the odds of having received palliative chemotherapy were also similar (OR 0.91, 95 % CI 0.55-1.51). Black and white patients with PDAC had a similar median overall survival. In a multivariate analysis, as compared to whites, black race was not associated with shorter overall survival. CONCLUSIONS: We observed no disparities in either management or survival between white and black patients with PDAC treated in the DoD's equal access health care system. These data suggest that improving the access of minorities with PDAC to health care may reduce disparities in their oncologic outcomes.

[53]

TÍTULO / TITLE: - Phase II Study of Induction Fixed-Dose Rate Gemcitabine and Bevacizumab Followed by 30 Gy Radiotherapy as Preoperative Treatment for Potentially Resectable Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Aug 1.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3161-9](#)

AUTORES / AUTHORS: - Van Buren G 2nd; Ramanathan RK; Krasinskas AM; Smith RP; Abood GJ; Bahary N; Lembersky BC; Shuai Y; Potter DM; Bartlett DL; Zureikat AH; James Moser A

INSTITUCIÓN / INSTITUTION: - Division of Surgical Oncology, UPMC Pancreatic Cancer Center, Pittsburgh, PA, USA.

RESUMEN / SUMMARY: - BACKGROUND: Eighty percent of patients with resected pancreatic ductal carcinoma (PDC) experience treatment failure within 2 years. We hypothesized that preoperative fixed-dose rate (FDR) gemcitabine (GEM) combined with the angiogenesis inhibitor bevacizumab (BEV) and accelerated 30 Gy radiotherapy (RT) would improve outcomes among patients with potentially resectable PDC. METHODS: This phase II trial tested induction FDR GEM (1,500 mg/m²) plus BEV (10

mg/kg IV) every 2 weeks for three cycles followed by accelerated RT (30 Gy in 10 fractions) plus BEV directed at gross tumor volume plus a 1-2 cm vascular margin. Subjects underwent laparoscopy and resection after day 85. Therapy was considered effective if the complete pathologic response rate exceeded 10 % and the margin-negative resection rate exceeded 80 %. RESULTS: Fifty-nine subjects were enrolled; 29 had potential portal vein involvement. Two grade 4 (3.4 %) and 19 grade 3 toxicities (32.8 %) occurred. Four subjects manifested radiographic progression, and 10 had undetected carcinomatosis. Forty-three pancreatic resections (73 %) were performed, including 19 portal vein resections (44 %). Margin-negative outcomes were observed in 38 (88 %, 95 % confidence interval [CI] 75-96), with one complete pathologic response (2.3 %; 95 % CI 0.1-12). There were seven (6 grade 3; 1 grade 4) wound complications (13 %). Median overall survival for the entire cohort was 16.8 months (95 % CI 14.9-21.3) and 19.7 months (95 % CI 16.5-28.2) after resection. CONCLUSIONS: Induction therapy with FDR GEM and BEV, followed by accelerated BEV/RT to 30 Gy, was well tolerated. Although both effectiveness criteria were achieved, survival outcomes were equivalent to published regimens.

[54]

TÍTULO / TITLE: - Modulation of c-kit expression in pancreatic adenocarcinoma: A novel stem cell marker responsible for the progression of the disease.

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

REVISTA / JOURNAL: - Acta Histochem. 2013 Aug 23. pii: S0065-1281(13)00141-4. doi: 10.1016/j.acthis.2013.07.002.

●● Enlace al texto completo (gratis o de pago) [1016/j.acthis.2013.07.002](#)

AUTORES / AUTHORS: - Amsterdam A; Raanan C; Polin N; Melzer E; Givol D; Schreiber L

INSTITUCIÓN / INSTITUTION: - Department of Molecular Cell Biology, The Weizmann Institute of Science, 234 Herzl Street, Rehovot 76100, Israel. Electronic address: Abraham.amsterdam@weizmann.ac.il.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancers because of late symptoms and resistance to chemotherapy and radiation therapy. We have investigated the appearance of c-kit, a stem cell marker, in both normal adult pancreatic tissue and in cancerous tissue. Apart from some very pale staining of islets of Langerhans, normal pancreas was devoid of staining with antibodies to c-kit. In contrast, in cancerous tissue that still preserves the overall integrity of the pancreatic tissue, there was a clear labeling in islets of Langerhans, which seemed to be co-localized with insulin containing beta cells. In other cases, where the pancreatic tissue was completely deteriorated, intensive labeling was clearly evident in remnants of both the exocrine and the endocrine tissues. The duct cells of the adenocarcinoma were moderately but clearly labeled with antibodies to c-kit. In contrast, in metastasis of PDAC, very intensive labeling of c-kit was evident. The

location of KRAS, which is strongly associated with PDAC, was also analyzed at the initial stages of the disease, when islets of Langerhans still preserve their integrity to a large extent. KRAS was found exclusively in islets of Langerhans and overlapped in its location with insulin and c-kit expressing cells. It is suggested that the modulation of the expression of c-kit, visualized by antibodies to the oncogene molecule, may play an important role in the formation and progression of PDAC. The absence of c-kit in normal pancreas and its appearance in PDAC is probably due to a mutational event, which probably allows conversion of the beta cells into cancer stem cells (CSC). Co-expression of both c-kit and KRAS, typical markers for CSC with overlapping with insulin in islets of Langerhans, strongly support the notion that beta-cells play a central role in the development of PDAC. The use of specific drugs that can attenuate the kinase activity of c-kit or target KRAS expressing cancer cells should be tested in order to attenuate the progression of this lethal disease.

[55]

TÍTULO / TITLE: - A rare finding of a rare disease: a case report of a giant insulinoma.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1195-6. doi: 10.1097/MPA.0b013e31829004d9.

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

[1097/MPA.0b013e31829004d9](#)

AUTORES / AUTHORS: - Fenech VA; Ellul P; Abela A; Caruana C; Cassar M; Laferla G

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology Mater Dei Hospital Malta valerie_fenech@yahoo.com Department of Diabetes and Endocrinology Mater Dei Hospital Malta Department of Surgery Mater Dei Hospital Malta.

[56]

TÍTULO / TITLE: - Pancreatic Intraepithelial Neoplasia in Patients With Intraductal Papillary Mucinous Neoplasms: The Interest of Endoscopic Ultrasonography.

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

REVISTA / JOURNAL: - Pancreas. 2013 Jul 30.

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

[1097/MPA.0b013e3182962723](#)

AUTORES / AUTHORS: - Maire F; Couvelard A; Palazzo L; Aubert A; Vullierme MP; Rebours V; Hammel P; Sauvanet A; Levy P; Ruszniewski P

INSTITUCIÓN / INSTITUTION: - From the *Pole des Maladies de l'Appareil Digestif, Hopital Beaujon, AP-HP; daggerUniversite Paris 7-Denis-Diderot; and double daggerService d'Anatomie Pathologique, and section signService de Radiologie, Hopital Beaujon, AP-HP, Clichy, France.

RESUMEN / SUMMARY: - OBJECTIVES: Intraductal papillary mucinous neoplasms (IPMNs) and pancreatic intraepithelial neoplasia (PanIN) are both precancerous lesions. Papillary mucinous neoplasms have been described in patients with IPMN, but their relationship is still poorly understood. The aims of this study were to look for PanIN lesions in patients operated on for IPMN and to search for correlations between endoscopic ultrasonography (EUS) features and pathologic findings. METHODS: Endoscopic ultrasonography was preoperatively performed in all patients with IPMN consecutively operated on in our center. Endoscopic ultrasonography features were prospectively compared with pathologic data from surgical specimen. RESULTS: Forty patients underwent resection for benign (52.5%) or malignant (47.5%) IPMN. Pancreatic intraepithelial neoplasia lesions were observed in 78% of cases (PanIN-3 in 19% of patients). PanIN-3 lesions were observed in 11% and 26% of patients with benign and malignant IPMN, respectively. Endoscopic ultrasonography changes (microcysts and/or hyperechoic foci) corresponded to PanIN lesions in 83% of cases. Endoscopic ultrasonography detected 69% of patients with PanIN lesions and 57% of those with panIN-3 lesions. CONCLUSIONS: Pancreatic intraepithelial neoplasia lesions are very frequently associated with IPMN, and 19% of patients with IPMN had PanIN-3 lesions. In two thirds of patients, EUS can detect minimal changes in the pancreas corresponding to PanIN lesions.

[57]

TÍTULO / TITLE: - Cathepsin B Contributes to Atg7-induced NLRP3 Dependent Pro-inflammatory Response and Aggravates Lipotoxicity in Rat Insulinoma Cell Line.

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

REVISTA / JOURNAL: - J Biol Chem. 2013 Aug 28.

●● Enlace al texto completo (gratis o de pago) [1074/jbc.M113.494286](https://doi.org/10.1074/jbc.M113.494286)

AUTORES / AUTHORS: - Li S; Du L; Zhang L; Hu Y; Xia W; Wu J; Zhu J; Chen L; Zhu F; Yang S

INSTITUCIÓN / INSTITUTION: - Nanjing Normal University, China.

RESUMEN / SUMMARY: - Abstract Impairment of glucose-stimulated insulin secretion (GSIS) caused by palmitate because of its lipotoxicity was found in beta cells. Recent studies have indicated that defects in autophagy contribute to pathogenesis in T2D. Here, we reported that autophagy related 7 (Atg7) induced excessive autophagic activation in INS-1(823/13) cells exposure to saturated fatty acids. Atg7-induced Cathepsin B (CTSB) overexpression resulted in unexpectedly significant increased pro-inflammatory chemokine and cytokine production level of IL-1beta, MCP-1, IL-6, and TNF-alpha. Inhibition receptor interacting protein (RIP1) did not affect inflammatory response ruling out involvement of necrosis. CTSB siRNA suppressed inflammatory response but did not affect apoptosis significantly suggested that CTSB was a molecular linker between autophagy and pro-inflammatory response. Blocking Caspase 3 suppressed apoptosis but did not affect inflammatory response suggested

that CTSB induced inflammatory effects independent of apoptosis. Silencing of the NLRP3 receptor, completely abolished IL-1beta secretion, and completely abolished the down-regulation effects of Atg7-induced CTSB overexpression on GSIS impairment, thus identifying NLRP3 inflammasome as autophagy-responsive element in pancreatic INS-1(823/13) cell line. Combined together, our results indicated that CTSB contributed to Atg7 induced NLRP3 dependent pro-inflammatory response resulted in lipotoxicity aggravation, independent of apoptosis in pancreatic INS-1(823/13) cell line.

[58]

TÍTULO / TITLE: - Lifetime adiposity and risk of pancreatic cancer in the NIH-AARP Diet and Health Study cohort.

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

REVISTA / JOURNAL: - Am J Clin Nutr. 2013 Oct;98(4):1057-65. doi: 10.3945/ajcn.113.058123. Epub 2013 Aug 28.

●● Enlace al texto completo (gratis o de pago) [3945/ajcn.113.058123](#)

AUTORES / AUTHORS: - Stolzenberg-Solomon RZ; Schairer C; Moore S; Hollenbeck A; Silverman DT

INSTITUCIÓN / INSTITUTION: - Branches of Nutritional Epidemiology, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Rockville, MD.

RESUMEN / SUMMARY: - BACKGROUND: The association of excess body weight across a lifetime with pancreatic cancer has not been examined extensively. OBJECTIVE: We determined the association for body mass index (BMI) at different ages and adiposity duration and gain with incident pancreatic adenocarcinoma in the NIH-AARP Diet and Health Study cohort. DESIGN: Participants aged 50-71 y completed questionnaires at baseline (1995-1996) and 6 months later that queried height and weight history. We calculated HRs and 95% CIs by using Cox proportional hazards models adjusted for age, smoking, sex, and intakes of energy and total fat. Results: Over an average follow-up of 10.5 y, 1206 and 2122 pancreatic cancer cases were identified in the subcohort who completed the second questionnaire (n = 273,975) and the baseline cohort (n = 501,698), respectively. Compared with normal weight, overweight or obesity at ages 18, 35, 50, or >50 y (baseline BMI) was significantly associated with pancreatic cancer, with HRs ranging from 1.15 to 1.53. A longer duration of BMI (in kg/m²) >25.0 was significantly associated with pancreatic cancer (overall HR per 10-y increment of duration: 1.06; 95% CI: 1.02, 1.09), with individuals who reported diabetes having the greatest risk (HR per 10-y increment of duration: 1.18; 95% CI: 1.05, 1.32; P-interaction = 0.01) and rates. A substantial gain in adiposity (>10 kg/m²) after age 50 y was significantly associated with increased pancreatic cancer risk. The etiologic fraction of pancreatic cancer explained by adiposity at any age was 14% overall and

21% in never smokers. CONCLUSION: Overweight and obesity at any age are associated with increased pancreatic cancer.

[59]

TÍTULO / TITLE: - Erlotinib-induced thrombocytosis in patients with recurrence of pancreatic cancer after distal pancreatectomy.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1196-7. doi: 10.1097/MPA.0b013e31828cf976.

●● Enlace al texto completo (gratis o de pago) [1097/MPA.0b013e31828cf976](#)

AUTORES / AUTHORS: - Uwagawa T; Misawa T; Fujiwara Y; Furukawa K; Tsutsui N; Kitamura H; Shiba H; Futagawa Y; Aiba K; Yanaga K

INSTITUCIÓN / INSTITUTION: - Department of Surgery and Department of Medical Oncology and Hematology The Jikei University School of Medicine Tokyo, Japan uwatadashi@msn.com Department of Surgery The Jikei University School of Medicine Tokyo, Japan Department of Medical Oncology and Hematology The Jikei University School of Medicine Tokyo, Japan Department of Surgery The Jikei University School of Medicine Tokyo, Japan.

[60]

TÍTULO / TITLE: - Association between single-nucleotide polymorphisms of OGG1 gene and pancreatic cancer risk in Chinese Han population.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Sep 3.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1111-6](#)

AUTORES / AUTHORS: - Chen H; Zhou B; Lan X; Wei D; Yuan T; Chen P

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, Daping Hospital, The Third Military Medical University, No. 10 Changjiangzhilu Daping, Chongqing, 400042, People's Republic of China.

RESUMEN / SUMMARY: - The purpose of this study was to test the association between single-nucleotide polymorphisms (SNPs) of 8-oxoguanine DNA glycosylase (OGG1) gene and susceptibility to pancreatic cancer (PC). A total of 347 PC patients and 364 healthy subjects were enrolled in this case-control study. The c.269C>A genetic variant was investigated using the created restriction site-polymerase chain reaction method. The c.627T>C genetic variant was identified by the polymerase chain reaction-restriction fragment length polymorphism method. Our data indicated that the alleles and genotypes frequencies of these two SNPs were statistically different in PC cases and controls. As for c.269C>A, the AA genotype was statistically associated with decreased PC susceptibility compared to CC wild genotype (odds ratio (OR) = 0.44, 95

% confidence interval (CI) 0.27-0.73, P = 0.001). As for c.627T>C, statistically significant decreased PC susceptibility was detected in CC genotype compared to TT wild genotype (OR = 0.57, 95 % CI 0.35-0.94, P = 0.028). The allele A of c.269C>A and allele C of c.627T>C might be associated with a protection from PC (for c.269C>A, A versus (vs.) C, OR = 0.69, 95 % CI 0.55-0.86, P < 0.001; for c.627T>C, C vs. T, OR = 0.72, 95 % CI 0.58-0.91, P = 0.005). Results from this study indicate that the c.269C>A and c.627T>C SNPs of OGG1 gene are associated with PC susceptibility in Chinese Han ethnicity.

[61]

TÍTULO / TITLE: - FOLFIRI in patients with locally advanced or metastatic pancreatic or biliary tract carcinoma: a monoinstitutional experience.

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

REVISTA / JOURNAL: - Anticancer Drugs. 2013 Oct;24(9):980-5. doi: 10.1097/CAD.0b013e328364e66b.

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

[1097/CAD.0b013e328364e66b](#)

AUTORES / AUTHORS: - Moretto R; Raimondo L; De Stefano A; Cella CA; Matano E; De Placido S; Carlomagno C

INSTITUCIÓN / INSTITUTION: - Department of Clinical Medicine and Surgery, Division of Medical Oncology, University 'Federico II' of Naples, Naples, Italy.

RESUMEN / SUMMARY: - Pancreatic and biliary tract carcinomas are very chemoresistant. After a first-line treatment with a gemcitabine-based regimen, no second-line scheme is consolidated in clinical practice. The aim of this study was to evaluate the toxicity and the activity of the FOLFIRI regimen as first-line or second-line chemotherapy in patients with pancreatic or biliary tract tumors. Fifty-four patients (30 with pancreatic tumor, nine with gallbladder tumor, and 15 with biliary tract tumor) were treated with FOLFIRI (irinotecan 180 mg/m, day 1; leucovorin 100 mg/m intravenously, days 1 and 2; 5-fluorouracil 400 mg/m intravenous bolus, days 1 and 2; and 600 mg/m in 22 h intravenously, continuous infusion days 1 and 2; every 14 days). Toxicity was recorded at each cycle according to the NCI-CTC V3.0 criteria, the response rate was verified each four cycles according to the RECIST criteria, and the progression-free survival rates as well as the overall survival rates were calculated according to the Kaplan-Meier method. Overall, the toxicity was mild. Grade 3-4 neutropenia occurred in 42.6% of patients. Grade 3-4 gastrointestinal toxicity was rare. FOLFIRI as a first-line treatment produced a response rate of 25%. In the second-line group, 9/21 patients (42.9%) obtained a stable disease as best response. In the entire population, the median progression-free survival rates were 3.1 months [95% confidence interval (CI), 1.9-4.4] and 3.5 months (95% CI, 2.6-4.4), respectively, in the first-line and the second-line cohort of patients. The median overall survival rates were 14.5 months (95% CI, 7.0-22.1) and 6.2 months (95% CI, 5.4-7.0), respectively, in the first-line and the

second-line cohort of patients. FOLFIRI is feasible and well tolerated in patients with pancreatic or biliary tract tumors; it has a good activity in first line and mostly in patients with pancreatic cancer.

[62]

TÍTULO / TITLE: - Comparing dose-volume histogram and radiobiological endpoints for ranking intensity-modulated arc therapy and 3D-radiotherapy treatment plans for locally-advanced pancreatic cancer.

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

REVISTA / JOURNAL: - Acta Oncol. 2013 Oct;52(7):1573-8. doi: 10.3109/0284186X.2013.813072. Epub 2013 Aug 19.

●● Enlace al texto completo (gratis o de pago) [3109/0284186X.2013.813072](#)

AUTORES / AUTHORS: - Warren S; Partridge M; Fokas E; Eccles CL; Brunner TB

INSTITUCIÓN / INSTITUTION: - The Gray Institute of Radiation Oncology and Biology, Department of Oncology, University of Oxford, Old Road Campus Research Building, Oxford, UK.

[63]

TÍTULO / TITLE: - Cell-Free Plasma MicroRNA in Pancreatic Ductal Adenocarcinoma and Disease Controls.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1107-13. doi: 10.1097/MPA.0b013e318296bb34.

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

[1097/MPA.0b013e318296bb34](#)

AUTORES / AUTHORS: - Carlsen AL; Joergensen MT; Knudsen S; de Muckadell OB; Heegaard NH

INSTITUCIÓN / INSTITUTION: - From the *Department of Clinical Biochemistry, Immunology & Genetics, Statens Serum Institut, Copenhagen; daggerDepartment of Medical Gastroenterology, Odense University Hospital, Odense; and double daggerMedical Prognosis Institute, Horsholm, Denmark.

RESUMEN / SUMMARY: - OBJECTIVES: There are no tumor-specific biochemical markers for pancreatic ductal adenocarcinoma (PDAC). Tissue-specific gene expression including microRNA (miRNA) profiling, however, identifies specific PDAC signatures. This study evaluates associations between circulating, cell-free plasma-miRNA profiles and PDAC in a disease and disease-control cohort. METHODS: We performed a microarray profiling of 847 different mature miRNAs from plasma in an exploratory cohort of 20 patients with PDAC or other pancreatic diseases, profiling of 45 miRNAs in plasma samples from PDAC (n = 48) and disease controls (n = 47), and evaluation of

associations of data with diagnosis, survival, and CA-19-9. RESULTS: We find 7 significantly deregulated miRNAs in PDAC using univariate statistics. At a false-discovery rate of 5%, miRNA-375 remained significantly elevated in PDAC. MicroRNA-375 did not improve diagnosis of PDAC in this cohort (70% accuracy) and did not correlate with survival. However, 3 controls (other gastrointestinal cancers) with increased CA-19-9 did not show increased miRNA-375. CONCLUSIONS: In the plasma-miRNA population, we find miRNA-375, which is selectively expressed in the endocrine pancreas under normal conditions, increased in PDAC cases compared with patients with other pancreatic or gastrointestinal diseases. The miRNA-375 does not outperform CA-19-9 diagnostically in the present cohort. However, it shows promising specificity and should be examined in larger prospective studies.

[64]

TÍTULO / TITLE: - Bortezomib-induced acute pancreatitis in a patient with multiple myeloma.

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

REVISTA / JOURNAL: - Leuk Lymphoma. 2013 Aug 28.

●● Enlace al texto completo (gratis o de pago) [3109/10428194.2013.831850](#)

AUTORES / AUTHORS: - Wang HH; Tsui J; Wang XY; Liu SS; Li J

INSTITUCIÓN / INSTITUTION: - Department of Hematology.

[65]

TÍTULO / TITLE: - miR-143 decreases COX-2 mRNA stability and expression in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Sep 13;439(1):6-11. doi: 10.1016/j.bbrc.2013.08.042. Epub 2013 Aug 21.

●● Enlace al texto completo (gratis o de pago) [1016/j.bbrc.2013.08.042](#)

AUTORES / AUTHORS: - Pham H; Ekaterina Rodriguez C; Donald GW; Hertzler KM; Jung XS; Chang HH; Moro A; Reber HA; Hines OJ; Eibl G

INSTITUCIÓN / INSTITUTION: - Department of Surgery, UCLA Center of Excellence in Pancreatic Diseases, UCLA David Geffen School of Medicine, University of California - Los Angeles, Los Angeles, CA 90095, United States; Department of Medicine, Veterans Affairs Greater Los Angeles Healthcare System, Los Angeles, CA 90073, United States.

RESUMEN / SUMMARY: - Small non-coding RNAs, microRNAs (miRNA), inhibit the translation or accelerate the degradation of message RNA (mRNA) by targeting the 3'-untranslated region (3'-UTR) in regulating growth and survival through gene suppression. Deregulated miRNA expression contributes to disease progression in several cancers types, including pancreatic cancers (PaCa). PaCa tissues and cells

exhibit decreased miRNA, elevated cyclooxygenase (COX)-2 and increased prostaglandin E2 (PGE2) resulting in increased cancer growth and metastases. Human PaCa cell lines were used to demonstrate that restoration of miRNA-143 (miR-143) regulates COX-2 and inhibits cell proliferation. miR-143 were detected at fold levels of 0.41+/-0.06 in AsPC-1, 0.20+/-0.05 in Capan-2 and 0.10+/-0.02 in MIA PaCa-2. miR-143 was not detected in BxPC-3, HPAF-II and Panc-1 which correlated with elevated mitogen-activated kinase (MAPK) and MAPK kinase (MEK) activation. Treatment with 10µM of MEK inhibitor U0126 or PD98059 increased miR-143, respectively, by 187+/-18 and 152+/-26-fold in BxPC-3 and 182+/-7 and 136+/-9-fold in HPAF-II. miR-143 transfection diminished COX-2 mRNA stability at 60min by 2.6+/-0.3-fold in BxPC-3 and 2.5+/-0.2-fold in HPAF-II. COX-2 expression and cellular proliferation in BxPC-3 and HPAF-II inversely correlated with increasing miR-143. PGE2 levels decreased by 39.3+/-5.0% in BxPC-3 and 48.0+/-3.0% in HPAF-II transfected with miR-143. Restoration of miR-143 in PaCa cells suppressed of COX-2, PGE2, cellular proliferation and MEK/MAPK activation, implicating this pathway in regulating miR-143 expression.

[66]

TÍTULO / TITLE: - Polymorphisms in metabolism/antioxidant genes may mediate the effect of dietary intake on pancreatic cancer risk.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1043-53. doi: 10.1097/MPA.0b013e3182968e00.

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

[1097/MPA.0b013e3182968e00](#)

AUTORES / AUTHORS: - Jansen RJ; Robinson DP; Stolzenberg-Solomon RZ; Bamlet WR; Tan X; Cunningham JM; Li Y; Rider DN; Oberg AL; Rabe KG; Anderson KE; Sinha R; Petersen GM

INSTITUCIÓN / INSTITUTION: - From the Divisions of *Epidemiology, and daggerBiomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, MN; double daggerDepartment of Epidemiology, National Institutes of Health, Bethesda, MD; section signDepartment of Epidemiology and Community Health, University of Minnesota, Minneapolis, MN; and parallelDivision of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD.

RESUMEN / SUMMARY: - OBJECTIVES: A source of variation for inconsistent dietary-pancreatic cancer associations may be individuals carrying constitutional metabolism/antioxidant gene variants that differentially benefit compared to homozygous individuals. Seventy-six tag single-nucleotide polymorphisms were genotyped in 13 candidate genes to test differential associations with pancreatic adenocarcinoma. METHODS: A clinic-based case-control design was used to rapidly ascertain 251 cases and 970 frequency matched controls who provided blood samples

and completed a 144-item food frequency questionnaire. Single-nucleotide polymorphisms were evaluated using a dominant genetic model and dietary categories split on controls' median intake. Logistic regression was used to calculate odds ratios and 95% confidence intervals, adjusted for potential confounders. RESULTS: Significant increased associations (Bonferroni corrected $P \leq 0.0007$) were observed for carriers of greater than or equal to 1 minor allele for rs3816257 (glucosidase, alpha; acid [GAA]) and lower intake of deep-yellow vegetables (1.90 [1.28-2.83]); and carriers of no minor allele for rs12807961 (catalase [CAT]) and high total grains intake (2.48 [1.50-4.09]), whereas those with greater than or equal to 1 minor allele had a decreasing slope (across grains). The reference group was no minor alleles with low dietary intake. CONCLUSIONS: Interindividual variation in metabolism/antioxidant genes could interact with dietary intake to influence pancreatic cancer risk.

[67]

TÍTULO / TITLE: - The pretreatment platelet and plasma fibrinogen level correlate with tumor progression and metastasis in patients with pancreatic cancer.

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

REVISTA / JOURNAL: - Platelets. 2013 Sep 3.

●● [Enlace al texto completo \(gratis o de pago\) 3109/09537104.2013.827782](#)

AUTORES / AUTHORS: - Wang H; Gao J; Bai M; Liu R; Li H; Deng T; Zhou L; Han R; Ge S; Huang D; Ba Y

INSTITUCIÓN / INSTITUTION: - Department of Gastrointestinal Medical Oncology, Tianjin Medical University Cancer Institute and Hospital, Key Laboratory of Cancer Prevention and Therapy, Tianjin, China.

RESUMEN / SUMMARY: - Abstract Cancer patients frequently present with activated coagulation pathways and thrombocytosis, which are potentially associated with tumor progression and prognosis. However, the prognostic value of abnormal plasma fibrinogen and platelet levels for the treatment of pancreatic cancer is unclear. The purpose of our study was to evaluate the prognostic value of plasma fibrinogen and platelet levels in pancreatic cancer, and to devise a prognostic model to identify the patients with greatest risk for a poor overall survival. One hundred and twenty-five patients diagnosed with pancreatic ductal adenocarcinoma in our hospital between May 2000 and June 2005 were included in this study. The plasma fibrinogen and platelet levels were examined before treatment and analyzed along with patient clinicopathological parameters and overall survival. The foundation of prognostic model was based on the risk factors according to the Cox proportional hazard model. The incidence of hyperfibrinogenemia and thrombocytosis was 24.8% (31/125) and 15.2% (19/125), respectively. The mean fibrinogen concentration differed significantly between the early (I/II) and late (III/IV) stage patients (3.19 +/- 0.70 vs. 3.65 +/- 0.90 g/l, $p = 0.008$). Patients with a higher concentration of plasma fibrinogen and platelets

had a worse prognosis ($p < 0.05$). There also existed a significant correlation between higher fibrinogen/platelet levels and distant organ metastasis ($p < 0.05$, respectively). Bivariate correlation analysis showed that plasma fibrinogen levels correlated significantly with platelet levels ($p = 0.000$). Multivariate analysis revealed that pretreatment plasma fibrinogen levels ($p = 0.027$), tumor stage ($p = 0.026$) and distant metastasis ($p = 0.027$) were independent prognostic factors. The median survival time for the low-, intermediate-, and high-risk groups was 9.6 months (95% CI 6.2-13.0), 3.8 months (95% CI 2.3-5.3), and 2.3 months (95% CI 0.9-3.7), respectively ($p = 0.000$). Pretreatment plasma fibrinogen and platelet levels closely correlated with tumor progression, metastasis and overall survival in pancreatic cancer. The foundation of prognostic model may help us identify the greatest risk populations with pancreatic cancer.

[68]

TÍTULO / TITLE: - Reproductive Factors, Exogenous Hormones, and Pancreatic Cancer Risk in the CTS.

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

REVISTA / JOURNAL: - Am J Epidemiol. 2013 Sep 12.

●● [Enlace al texto completo \(gratis o de pago\) 1093/aje/kwt154](#)

AUTORES / AUTHORS: - Lee E; Horn-Ross PL; Rull RP; Neuhausen SL; Anton-Culver H; Ursin G; Henderson KD; Bernstein L

RESUMEN / SUMMARY: - Female steroid hormones are hypothesized to play a protective role in pancreatic cancer risk. However, results from epidemiologic studies that examined hormone-related exposures have been inconsistent. The California Teachers Study is a cohort study of female public school professionals that was established in 1995-1996. Of the 118,164 eligible study participants, 323 women were diagnosed with incident invasive pancreatic cancer through December 31, 2009. Multivariable Cox proportional hazards regression methods were used to estimate hazard ratios and 95% confidence intervals for the association of pancreatic cancer risk with reproductive factors and exogenous hormone use. Current users of estrogen-only therapy at baseline (1995-1996) had a lower risk of pancreatic cancer than did participants who had never used hormone therapy (hazard ratio = 0.59, 95% confidence interval: 0.42, 0.84). Use of estrogen-plus-progestin therapy was not associated with the risk of pancreatic cancer. A longer duration of oral contraceptive use (≥ 10 years of use compared with never use) was associated with an increased risk of cancer (hazard ratio = 1.72, 95% confidence interval: 1.19, 2.49). Reproductive factors, including age at menarche, parity, breastfeeding, and age at menopause, were not associated with pancreatic cancer risk. Our results suggest that increased estrogen exposure through estrogen-only therapy may reduce pancreatic cancer risk in women.

[69]

TÍTULO / TITLE: - Demyelinating neuropathy and autoimmune hemolytic anemia in a patient with pancreatic cancer.

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

REVISTA / JOURNAL: - Intern Med. 2013;52(15):1737-40. Epub 2012 Mar 1.

AUTORES / AUTHORS: - Koike H; Yoshida H; Ito T; Ohyama K; Hashimoto R; Kawagashira Y; Iijima M; Sobue G

INSTITUCIÓN / INSTITUTION: - Department of Neurology, Nagoya University Graduate School of Medicine, Japan.

RESUMEN / SUMMARY: - We herein report the case of a patient with pancreatic cancer who manifested features of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and autoimmune hemolytic anemia (AIHA). A 78-year-old Japanese man presented with AIHA and was treated with steroids and splenectomy. Although the AIHA improved following splenectomy, the patient suffered from sensorimotor neuropathy soon after undergoing surgery. The electrophysiological features indicated demyelinating neuropathy. The neuropathy was refractory to immunomodulatory treatment, and intensive investigations revealed pancreatic cancer. The patient's neurological deficits improved significantly after the surgery for cancer. Although the combination of AIHA and CIDP has been reported anecdotally, this is the first case of the coexistence of these diseases as paraneoplastic syndromes.

[70]

TÍTULO / TITLE: - PPAPDC1B and WHSC1L1 Are Common Drivers of the 8p11-12 Amplicon, Not Only in Breast Tumors But also in Pancreatic Adenocarcinomas and Lung Tumors.

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

REVISTA / JOURNAL: - Am J Pathol. 2013 Sep 17. pii: S0002-9440(13)00552-X. doi: 10.1016/j.ajpath.2013.07.028.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.ajpath.2013.07.028](#)

AUTORES / AUTHORS: - Mahmood SF; Gruel N; Nicolle R; Chapeaublanc E; Delattre O; Radvanyi F; Bernard-Pierrot I

INSTITUCIÓN / INSTITUTION: - Centre National de la Recherche Scientifique, UMR 144, Institut Curie, Paris, France; Research Center, Institut Curie, Paris, France.

RESUMEN / SUMMARY: - Amplification of the 8p11-12 chromosomal region is a common genetic event in many epithelial cancers. In breast cancer, several genes within this region have been shown to display oncogenic activity. Among these genes, the enzyme-encoding genes, PPAPDC1B and WHSC1L1, have been identified as potential therapeutic targets. We investigated whether PPAPDC1B and WHSC1L1 acted as

general driver genes, thereby serving as therapeutic targets in other tumors with 8p11-12 amplification. By using publicly available genomic data from a panel of 883 cell lines derived from different cancers, we identified the cell lines presenting amplification of both WHSC1L1 and PPAPDC1B. In particular, we focused on cell lines derived from lung cancer and pancreatic adenocarcinoma and found a correlation between the amplification of PPAPDC1B and WHSC1L1 with their overexpression. Loss-of-function studies based on the use of siRNA and shRNA demonstrated that PPAPDC1B and WHSC1L1 played a major role in regulating the survival of pancreatic adenocarcinoma and small-cell lung cancer-derived cell lines, both in anchorage-dependent and anchorage-independent conditions, displaying amplification and overexpression of these genes. We also demonstrated that PPAPDC1B and WHSC1L1 regulated xenograft growth in these cell lines. Finally, quantitative RT-PCR experiments after PPAPDC1B and WHSC1L1 knockdown revealed exclusive PPAPDC1B and WHSC1L1 gene targets in small-cell lung cancer and pancreatic adenocarcinoma-derived cell lines compared with breast cancer.

[71]

TÍTULO / TITLE: - Genetic inactivation of Nupr1 acts as a dominant suppressor event in a two-hit model of pancreatic carcinogenesis.

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

REVISTA / JOURNAL: - Gut. 2013 Sep 14. doi: 10.1136/gutjnl-2013-305221.

●● [Enlace al texto completo \(gratis o de pago\) 1136/gutjnl-2013-305221](#)

AUTORES / AUTHORS: - Cano CE; Hamidi T; Garcia MN; Loncle C; Garcia S; Calvo E; Lomberk G; Dusetti N; Bartholin L; Urrutia R; Iovanna JL

INSTITUCIÓN / INSTITUTION: - Centre de Recherche en Carcerologie de Marseille (CRCM), INSERM UMR 1068, CNRS UMR 7258, Aix-Marseille University and Institut Paoli-Calmettes, Parc Scientifique et Technologique de Luminy, , Marseille, France.

RESUMEN / SUMMARY: - BACKGROUND: Nuclear protein 1 (Nupr1) is a major factor in the cell stress response required for KrasG12D-driven formation of pancreatic intraepithelial neoplastic lesions (PanINs). We evaluated the relevance of Nupr1 in the development of pancreatic cancer. METHODS: We investigated the role of Nupr1 in pancreatic ductal adenocarcinoma (PDAC) progression beyond PanINs in Pdx1-cre;LSL-KrasG12D;Ink4a/Arffl/fl(KIC) mice. RESULTS: Even in the context of the second tumorigenic hit of Ink4a/Arf deletion, Nupr1 deficiency led to suppression of malignant transformation involving caspase 3 activation in premalignant cells of KIC pancreas. Only half of Nupr1-deficient;KIC mice achieved PDAC development, and incident cases survived longer than Nupr1wt;KIC mice. This was associated with the development of well-differentiated PDACs in Nupr1-deficient;KIC mice, which displayed enrichment of genes characteristic of the recently identified human classical PDAC subtype. Nupr1-deficient;KIC PDACs also shared with human classical PDACs the overexpression of the

Kras-activation gene signature. In contrast, Nupr1wt;KIC mice developed invasive PDACs with enriched gene signature of human quasi-mesenchymal (QM) PDACs. Cells derived from Nupr1-deficient;KIC PDACs growth in an anchorage-independent manner in vitro had higher aldehyde dehydrogenase activity and overexpressed nanog, Oct-4 and Sox2 transcripts compared with Nupr1wt;KIC cells. Moreover, Nupr1-deficient and Nupr1wt;KIC cells differed in their sensitivity to the nucleoside analogues Ly101-4b and WJQ63. Together, these findings show the pivotal role of Nupr1 in both the initiation and late stages of PDAC in vivo, with a potential impact on PDAC cell stemness. CONCLUSIONS: According to Nupr1 status, KIC mice develop tumours that phenocopy human classical or QM-PDAC, respectively, and present differential drug sensitivity, thus becoming attractive models for preclinical drug trials.

[72]

TÍTULO / TITLE: - Absence of FLICE-Inhibitory Protein Is a Novel Independent Prognostic Marker for Very Short Survival in Pancreatic Ductal Adenocarcinoma.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1114-9. doi: 10.1097/MPA.0b013e31829655ed.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/MPA.0b013e31829655ed](#)

AUTORES / AUTHORS: - Schmid SJ; Glatzel MC; Welke C; Kornmann M; Kleger A; Barth TF; Fulda S; Lennerz JK; Moller P

INSTITUCIÓN / INSTITUTION: - From the *Department of Pathology, daggerComprehensive Cancer Center Ulm, and Departments of double daggerGeneral, Visceral and Transplantation Surgery and section signInternal Medicine, University Hospital Ulm, Germany; and parallelInstitute for Experimental Cancer Research in Pediatrics, Goethe-University Frankfurt, Germany.

RESUMEN / SUMMARY: - OBJECTIVES: Evading apoptosis is a hallmark of pancreatic cancer. In pancreatic cancer models, chemotherapy down-regulates the antiapoptotic protein cellular FLICE inhibitory protein (c-FLIP), which renders cells sensitive to apoptosis. Currently, the relevance of c-FLIP expression as a biomarker in pancreatic cancer is unknown, and here we assessed the prognostic significance of the c-FLIP expression status in a large cohort of pancreatic cancer patients with clinical follow-up. METHODS: Cellular FLICE inhibitory protein expression levels were determined by immunohistochemistry in 120 surgically resected ductal pancreatic adenocarcinomas. Survival analysis by c-FLIP status was compared with established clinicopathologic biomarkers as well as Ki-67 and cyclooxygenase 2 expression levels as 2 other established independent prognostic biomarkers in pancreatic cancer. RESULTS: Of 120 tumors, 111 (91%) were c-FLIP positive, whereas 9 (9%) were completely c-FLIP negative. Cyclooxygenase 2 was positive in 59 cases (52%), and Ki-67 was positive in

more than 10% of tumor cells in 51 cases (44%). Univariate and multivariate survival analysis (correcting for stage, grade, and proliferation index) showed that c-FLIP is an independent prognostic factor. Specifically, c-FLIP negativity identifies 9% of patients with a highly aggressive disease course (P = 0.0001). CONCLUSIONS: Cellular FLICE inhibitory protein expression status is a valuable prognostic biomarker in pancreatic cancer.

[73]

TÍTULO / TITLE: - Characterization of gene expression and activated signaling pathways in solid-pseudopapillary neoplasm of pancreas.

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

REVISTA / JOURNAL: - Mod Pathol. 2013 Sep 27. doi: 10.1038/modpathol.2013.154.

●● Enlace al texto completo (gratis o de pago) [1038/modpathol.2013.154](#)

AUTORES / AUTHORS: - Park M; Kim M; Hwang D; Park M; Kim WK; Kim SK; Shin J; Park ES; Kang CM; Paik YK; Kim H

INSTITUCIÓN / INSTITUTION: - Departments of Pathology and BK21 for Medical Science, Yonsei University College of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - Solid-pseudopapillary neoplasm is an uncommon pancreatic tumor with distinct clinicopathologic features. Solid-pseudopapillary neoplasms are characterized by mutations in exon 3 of CTNNB1. However, little is known about the gene and microRNA expression profiles of solid-pseudopapillary neoplasms. Thus, we sought to characterize solid-pseudopapillary neoplasm-specific gene expression and identify the signaling pathways activated in these tumors. Comparisons of gene expression in solid-pseudopapillary neoplasm to pancreatic ductal carcinomas, neuroendocrine tumors, and non-neoplastic pancreatic tissues identified solid-pseudopapillary neoplasm-specific mRNA and microRNA profiles. By analyzing 1686 (1119 upregulated and 567 downregulated) genes differentially expressed in solid-pseudopapillary neoplasm, we found that the Wnt/beta-catenin, Hedgehog, and androgen receptor signaling pathways, as well as genes involved in epithelial mesenchymal transition, are activated in solid-pseudopapillary neoplasms. We validated these results experimentally by assessing the expression of beta-catenin, WIF-1, GLI2, androgen receptor, and epithelial-mesenchymal transition-related markers with western blotting and immunohistochemistry. Our analysis also revealed 17 microRNAs, especially the miR-200 family and miR-192/215, closely associated with the upregulated genes associated with the three pathways activated in solid-pseudopapillary neoplasm and epithelial mesenchymal transition. Our results provide insight into the molecular mechanisms underlying solid-pseudopapillary neoplasm tumorigenesis and its characteristic less epithelial cell differentiation than the other common pancreatic tumors. Modern Pathology advance online publication, 27 September 2013; doi:10.1038/modpathol.2013.154.

[74]

TÍTULO / TITLE: - PIAS4 is an activator of hypoxia signalling via VHL suppression during growth of pancreatic cancer cells.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Oct 1;109(7):1795-1804. doi: 10.1038/bjc.2013.531. Epub 2013 Sep 3.

●● Enlace al texto completo (gratis o de pago) [1038/bjc.2013.531](#)

AUTORES / AUTHORS: - Chien W; Lee KL; Ding LW; Wuensche P; Kato H; Doan NB; Poellinger L; Said JW; Koeffler HP

INSTITUCIÓN / INSTITUTION: - Cancer Science Institute of Singapore, National University of Singapore, 14 Medical Drive, Level 12-01, Singapore 117599, Singapore.

RESUMEN / SUMMARY: - Background:The PIAS4 protein belongs to the family of protein inhibitors of activated STAT, but has since been implicated in various biological activities including the post-translational modification known as sumoylation. In this study, we explored the roles of PIAS4 in pancreatic tumorigenesis.Methods:The expression levels of PIAS4 in pancreatic cancer cells were examined. Cell proliferation and invasion was studied after overexpression and gene silencing of PIAS4. The effect of PIAS4 on hypoxia signalling was investigated.Results:The protein was overexpressed in pancreatic cancer cells compared with the normal pancreas. Gene silencing by PIAS4 small interfering RNA (siRNA) suppressed pancreatic cancer cell growth and overexpression of PIAS4 induced expression of genes related to cell growth. The overexpression of PIAS4 is essential for the regulation of the hypoxia signalling pathway. PIAS4 interacts with the tumour suppressor von Hippel-Lindau (VHL) and leads to VHL sumoylation, oligomerization, and impaired function. Pancreatic cancer cells (Panc0327, MiaPaCa2) treated with PIAS4 siRNA suppressed expression of the hypoxia-inducible factor hypoxia-inducible factor 1 alpha and its target genes JMJD1A, VEGF, and STAT3.Conclusion:Our study elucidates the role of PIAS4 in the regulation of pancreatic cancer cell growth, where the suppression of its activity represents a novel therapeutic target for pancreatic cancers.

[75]

TÍTULO / TITLE: - Aberrant Expression miR-196^a Is Associated With Abnormal Apoptosis, Invasion, and Proliferation of Pancreatic Cancer Cells.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1169-81. doi: 10.1097/MPA.0b013e3182962acb.

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

[1097/MPA.0b013e3182962acb](#)

AUTORES / AUTHORS: - Liu M; Du Y; Gao J; Liu J; Kong X; Gong Y; Li Z; Wu H; Chen H

INSTITUCIÓN / INSTITUTION: - From the Department of Gastroenterology, Changhai Hospital, Second Military Medical University, Shanghai, China.

RESUMEN / SUMMARY: - OBJECTIVES: miR-196^a levels inversely correlated with survival in pancreatic adenocarcinoma patients. However, the functional contributions of miR-196^a to pancreatic cancer remain unclear. METHODS: Three lentiviral vectors encoding microRNA miR-196^a precursor, inhibitor, and scrambled microRNA oligomer were transfected into Panc-1 cells, respectively. Then we explored the regulation of inhibitor of growth 5 (ING5) expression by miR-196^a and its impact on apoptosis, invasion, and growth of pancreatic cancer cells. The lentiviral transfected Panc-1 cells were surgically implanted into the pancreas of mice. In vivo tumor growth and ING5 expression were measured. RESULTS: Down-regulation of ING5 expression was detected in cells transfected with miR-196^a precursor (P < 0.01), accompanied by less apoptosis, increased invasion, and proliferation compared with control cells (P < 0.05). Cells transfected with miR-196^a inhibitor revealed an opposite trend. Smaller detectable tumors were found in only 60% of mice after implantation of Lenti.miR-196^a inhibitor-transfected Panc-1 cells compared with controls (360.7 +/- 303.6 mm vs 511.58 +/- 365.9 mm in controls; P < 0.01). CONCLUSION: Our results provide experimental evidence to support aberrant expression of miR-196^a is associated with abnormal apoptosis, invasion, and proliferation of pancreatic cancer cells.

[76]

TÍTULO / TITLE: - Ulcer, gastric surgery and pancreatic cancer risk: an analysis from the International Pancreatic Cancer Case-Control Consortium (PanC4).

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

REVISTA / JOURNAL: - Ann Oncol. 2013 Aug 22.

●● [Enlace al texto completo \(gratis o de pago\) 1093/annonc/mdt336](#)

AUTORES / AUTHORS: - Bosetti C; Lucenteforte E; Bracci PM; Negri E; Neale RE; Risch HA; Olson SH; Gallinger S; Miller AB; Bueno-de-Mesquita HB; Talamini R; Polesel J; Ghadirian P; Baghurst PA; Zatonski W; Fontham E; Holly EA; Gao YT; Yu H; Kurtz RC; Cotterchio M; Maisonneuve P; Zeegers MP; Duell EJ; Boffetta P; La Vecchia C

INSTITUCIÓN / INSTITUTION: - Department of Epidemiology, IRCCS, Istituto di Ricerche Farmacologiche 'Mario Negri', Milan.

RESUMEN / SUMMARY: - BACKGROUND: Peptic ulcer and its treatments have been associated to pancreatic cancer risk, although the evidence is inconsistent. METHODS: We pooled 10 case-control studies within the Pancreatic Cancer Case-control Consortium (PanC4), including 4717 pancreatic cancer cases and 9374 controls, and estimated summary odds ratios (OR) using multivariable logistic regression models. RESULTS: The OR for pancreatic cancer was 1.10 [95% confidence interval (CI) 0.98-1.23] for history of ulcer (OR = 1.08 for gastric and 0.97 for duodenal ulcer). The

association was stronger for a diagnosis within 2 years before cancer diagnosis (OR = 2.43 for peptic, 1.75 for gastric, and 1.98 for duodenal ulcer). The OR was 1.53 (95% CI 1.15-2.03) for history of gastrectomy; however, the excess risk was limited to a gastrectomy within 2 years before cancer diagnosis (OR = 6.18, 95% CI 1.82-20.96), while no significant increased risk was observed for longer time since gastrectomy. No associations were observed for pharmacological treatments for ulcer, such as antacids, H2-receptor antagonists, or proton-pump inhibitors. CONCLUSIONS: This uniquely large collaborative study does not support the hypothesis that peptic ulcer and its treatment materially affect pancreatic cancer risk. The increased risk for short-term history of ulcer and gastrectomy suggests that any such association is due to increased cancer surveillance.

[77]

TÍTULO / TITLE: - Molecular Targeted Therapy in Enteropancreatic Neuroendocrine Tumors: from Biology to Clinical Practice.

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

REVISTA / JOURNAL: - Curr Med Chem. 2013 Aug 23.

AUTORES / AUTHORS: - Fazio N; Scarpa A; Falconi M

INSTITUCIÓN / INSTITUTION: - Unit of Gastrointestinal and Neuroendocrine Tumor, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy.

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RESUMEN / SUMMARY: - Advanced enteropancreatic (EP) neuroendocrine tumors (NETs) can be treated with several different therapies, including chemotherapy, biotherapy, and locoregional treatments. Over the last few decades, impressive progress has been made in the biotherapy field. Three main druggable molecular targets have been studied and developed in terms of therapy: somatostatin receptor (sstr), mammalian target of rapamycin (mTOR), and angiogenic factors. In particular, research has moved from the old somatostatin analogs (SSAs), such as octreotide (OCT) and lanreotide (LAN), specifically binding to the sstr-2, to the newer pasireotide (PAS), which presents a wider sstr spectrum. Over the last ten years, several molecular targeted agents (MTAs) have been studied in phase II trials, and very few of them have reached phase III. The mTOR inhibitor everolimus and the multitargeted inhibitor sunitinib have been approved for clinical use by the FDA and EMA in advanced well/moderately-differentiated (WD, MD) progressive pancreatic neuroendocrine tumors (PNETs), on the basis of the positive results of two international large randomized phase III trials vs. placebo. Bevacizumab has been studied in a large US phase III trial vs. interferon (IFN)-alfa2b, and results are pending. In this review, the biological and clinical aspects of MTAs introduced into clinical practice or which are currently in an advanced phase of clinical investigation are addressed.

[78]

TÍTULO / TITLE: - Family History of Diabetes and Pancreatic Cancer as Risk Factors for Pancreatic Cancer: The PACIFIC Study.

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

REVISTA / JOURNAL: - Cancer Epidemiol Biomarkers Prev. 2013 Aug 21.

●● Enlace al texto completo (gratis o de pago) [1158/1055-9965.EPI-13-0518](#)

AUTORES / AUTHORS: - Austin MA; Kuo E; Van Den Eeden SK; Mandelson MT; Brentnall TA; Kamineneni A; Potter JD

INSTITUCIÓN / INSTITUTION: - Epidemiology, University of Washington.

RESUMEN / SUMMARY: - Genetic association studies have identified more than a dozen genes associated with risk of pancreatic cancer. Given this genetic heterogeneity, family history can be useful for identifying individuals at high-risk for this disease. The goal of this analysis was to evaluate associations of family history of diabetes and family history of pancreatic cancer with risk of pancreatic cancer. PACIFIC is a case-control study based in two large health plans. Cases were diagnosed with pancreatic ductal adenocarcinoma (PDA) and controls were selected from the health plan enrollment databases and frequency-matched to cases. Family history data were collected using an interviewer-administered questionnaire and were available on 654 cases and 697 controls. Logistic regression was used for the association analyses. First-degree relative history of diabetes was statistically significantly associated with increased risk of PDA (odds ratio (OR): 1.37, 95% confidence interval (CI): 1.10-1.71). The highest risk of PDA was observed for an offspring with diabetes (OR: 1.95, 95% CI: 1.23-3.09). In addition, history of pancreatic cancer increased risk for PDA with an OR of 2.79 (95% CI: 1.44-4.08) for any first-degree relative history of pancreatic cancer. This population-based analysis demonstrated that family history of diabetes was associated with increased risk of PDA, and confirmed previous studies showing that first-degree family history of pancreatic cancer is associated with PDA. These results support need for ongoing studies of genetic influences on pancreatic cancer in large samples and investigations of possible pleiotropic genetic effects on diabetes and pancreatic cancer.

[79]

TÍTULO / TITLE: - Hypoxia-Induced Snail Expression Through Transcriptional Regulation by HIF-1alpha in Pancreatic Cancer Cells.

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

REVISTA / JOURNAL: - Dig Dis Sci. 2013 Aug 25.

●● Enlace al texto completo (gratis o de pago) [1007/s10620-013-2841-4](#)

AUTORES / AUTHORS: - Zhu GH; Huang C; Feng ZZ; Lv XH; Qiu ZJ

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Fengxian Central Hospital, Shanghai, 201400, China, zhuzhu19820515@126.com.

RESUMEN / SUMMARY: - BACKGROUND: Intratumoral hypoxia and epithelial-mesenchymal transition are involved in tumor invasion and metastasis. AIMS: This study investigated the molecular mechanisms that relay the hypoxia signal into the epithelial-mesenchymal transition and metastasis. METHODS: Morphology analysis and tumor cell migration and invasion assays were performed to detect phenotypic changes of pancreatic cancer cells under normoxic and hypoxic conditions after lentiviral HIF-1alpha shRNA transfection. Quantitative reverse transcription polymerase chain reaction, western blot, and immunohistochemistry were used to detect gene expression in pancreatic cancer cell lines and tissues or normal pancreatic tissues. Luciferase, gel shift, and ChIP assays were used to assess gene regulation. RESULTS: Under hypoxic conditions, these tumor cells underwent typical morphological and molecular changes to epithelial-mesenchymal transition. Moreover, Snail expression was induced by hypoxic conditions and was regulated by HIF-1alpha expression at the transcriptional level through HIF-1alpha-binding to the second site of hypoxia-responsive elements of the Snail gene promoter. In addition, Snail expression was associated with HIF-1alpha expression in pancreatic cancer tissues, and expression of both was associated with tumor metastasis and poor patient survival. CONCLUSIONS: Our study provides key evidence that HIF-1alpha and Snail are responsible for hypoxia-induced metastasis phenotypes in pancreatic cancer and that HIF-1alpha and Snail expression can be used as biomarkers to predict tumor metastasis and patient survival.

[80]

TÍTULO / TITLE: - Large Solid-pseudopapillary Neoplasm of the Pancreas with Aberrant Protein Expression and Mutation of beta-Catenin: A Case Report and Literature Review of the Distribution of beta-Catenin Mutation.

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

REVISTA / JOURNAL: - Intern Med. 2013;52(18):2051-6.

AUTORES / AUTHORS: - Kobayashi T; Ozasa M; Miyashita K; Saga A; Miwa K; Saito M; Morioka M; Takeuchi M; Takenouchi N; Yabiku T; Kanno H; Yuzawa S; Tanino M; Tanaka S; Kawakami H; Asaka M; Sakamoto N

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Hokkaido University, Graduate School of Medicine, Japan.

RESUMEN / SUMMARY: - Solid-pseudopapillary neoplasms (SPN) are rare pancreatic tumors. The etiology of SPN involves mutations in the gene that encodes beta-catenin (CTNNB1). We herein report the case of a 23-year-old woman with a large SPN with proliferating tumor cells that displayed both solid and pseudo-papillary patterns. The simultaneous nuclear accumulation and loss of membrane localization of beta-catenin

and E-cadherin was specifically observed in the tumor cells. Further, the tumor cells were shown to harbor a missense mutation in exon 3 of CTNNB1. We also present a review of the literature describing the clustering of CTNNB1 mutations in patients with SPN.

[81]

TÍTULO / TITLE: - Early epigenetic downregulation of WNK2 kinase during pancreatic ductal adenocarcinoma development.

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

REVISTA / JOURNAL: - Oncogene. 2013 Aug 5. doi: 10.1038/onc.2013.312.

●● [Enlace al texto completo \(gratis o de pago\) 1038/onc.2013.312](#)

AUTORES / AUTHORS: - Dutruel C; Bergmann F; Rومان I; Zucknick M; Weichenhan D; Geiselhart L; Kaffenberger T; Rachakonda PS; Bauer A; Giese N; Hong C; Xie H; Costello JF; Hoheisel J; Kumar R; Rehli M; Schirmacher P; Werner J; Plass C; Popanda O; Schmezer P

INSTITUCIÓN / INSTITUTION: - Division of Epigenomics and Cancer Risk Factors, German Cancer Research Center (DKFZ), Heidelberg, Germany.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is usually incurable. Contrary to genetic mechanisms involved in PDAC pathogenesis, epigenetic alterations are ill defined. Here, we determine the contribution of epigenetically silenced genes to the development of PDAC. We analyzed enriched, highly methylated DNAs from PDACs, chronic pancreatitis (CP) and normal tissues using CpG island microarrays and identified WNK2 as a prominent candidate tumor suppressor gene being downregulated early in PDAC development. WNK2 was further investigated in tissue microarrays, methylation analysis of early pancreatic intraepithelial neoplasia (PanIN), mouse models for PDAC and pancreatitis, re-expression studies after demethylation, and cell growth assays using WNK2 overexpression. Demethylation assays confirmed the link between methylation and expression. WNK2 hypermethylation was higher in tumor than in surrounding inflamed tissues and was observed in PanIN lesions as well as in a PDAC mouse model. WNK2 mRNA and protein expressions were lower in PDAC and CP compared with normal tissues both in patients and mouse models. Overexpression of WNK2 led to reduced cell growth, and WNK2 expression in tissues correlated negatively with pERK1/2 expression, a downstream target of WNK2 responsible for cell proliferation. Downregulation of WNK2 by promoter hypermethylation occurs early in PDAC pathogenesis and may support tumor cell growth via the ERK-MAPK pathway. Oncogene advance online publication, 5 August 2013; doi:10.1038/onc.2013.312.

[82]

TÍTULO / TITLE: - Evaluating comparative effectiveness with observational data: Endoscopic ultrasound and survival in pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer. 2013 Aug 6. doi: 10.1002/cncr.28295.

●● Enlace al texto completo (gratis o de pago) [1002/cncr.28295](#)

AUTORES / AUTHORS: - Parmar AD; Sheffield KM; Han Y; Vargas GM; Guturu P; Kuo YF; Goodwin JS; Riall TS

INSTITUCIÓN / INSTITUTION: - Departments of Surgery, University of Texas Medical Branch, Galveston, Texas; University of California, San Francisco-East Bay, Oakland, California.

RESUMEN / SUMMARY: - BACKGROUND: A previous observational study reported that endoscopic ultrasound (EUS) is associated with improved survival in older patients with pancreatic cancer. The objective of this study was to reevaluate this association using different statistical methods to control for confounding and selection bias. METHODS: Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data (1992-2007) was used to identify patients with locoregional pancreatic cancer. Two-year survival in patients who did and did not receive EUS was compared by using standard Cox proportional hazards models, propensity score methodology, and instrumental variable analysis. RESULTS: EUS was associated with improved survival in both unadjusted (hazard ratio [HR] = 0.67, 95% confidence interval [CI] = 0.63-0.72) and standard regression analyses (HR = 0.78, 95% CI = 0.73-0.84) which controlled for age, sex, race, marital status, tumor stage, SEER region, Charlson comorbidity, year of diagnosis, education, preoperative biliary stenting, chemotherapy, radiation, and pancreatic resection. Propensity score adjustment, matching, and stratification did not attenuate this survival benefit. In an instrumental variable analysis, the survival benefit was no longer observed (HR = 1.00, 95% CI = 0.73-1.36). CONCLUSIONS: These results demonstrate the need to exercise caution in using administrative data to infer causal mortality benefits with diagnostic and/or treatment interventions in cancer research. Cancer 2013. © 2013 American Cancer Society.

[83]

TÍTULO / TITLE: - Dietary energy density is positively associated with risk of pancreatic cancer in urban shanghai chinese.

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

REVISTA / JOURNAL: - J Nutr. 2013 Oct;143(10):1626-9. doi: 10.3945/jn.113.178129. Epub 2013 Jul 31.

●● Enlace al texto completo (gratis o de pago) [3945/jn.113.178129](#)

AUTORES / AUTHORS: - Wang J; Zhang W; Sun L; Yu H; Ni QX; Risch HA; Gao YT

INSTITUCIÓN / INSTITUTION: - Department of Epidemiology, Shanghai Cancer Institute, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China.

RESUMEN / SUMMARY: - Regular consumption of energy-dense foods predisposes to obesity and type 2 diabetes, both of which are suggested risk factors for pancreatic cancer. The aim of this study was to investigate whether energy density of foods is an independent risk factor for pancreatic cancer. In this population-based case-control study in urban Shanghai, 908 patients with pancreatic cancer and 1067 normal controls, aged 35-79 y, were recruited. The energy density for overall diet was calculated from food-frequency questionnaire data. Energy density (adjusted for age, sex, and total energy intake) was significantly higher in cases (6.08 +/- 0.04 kJ/g) than in controls (5.91 +/- 0.04 kJ/g) (P = 0.003). Energy density was positively associated with pancreatic cancer risk (OR: 1.16 per unit increase; 95% CI: 1.07, 1.27; P < 0.001). In adjusted analysis, the risk of pancreatic cancer was 72% greater (OR: 1.72; 95% CI: 1.25, 2.35; P = 0.001) in the highest quintile of energy density compared with the lowest quintile. In this case-control study, dietary energy density is positively associated with risk of pancreatic cancer. This association should be further investigated in prospective studies.

[84]

TÍTULO / TITLE: - S100A4 mRNA expression level is a predictor of radioresistance of pancreatic cancer cells.

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

REVISTA / JOURNAL: - Oncol Rep. 2013 Oct;30(4):1601-8. doi: 10.3892/or.2013.2636. Epub 2013 Jul 24.

●● Enlace al texto completo (gratuito o de pago) [3892/or.2013.2636](#)

AUTORES / AUTHORS: - Kozono S; Ohuchida K; Ohtsuka T; Cui L; Eguchi D; Fujiwara K; Zhao M; Mizumoto K; Tanaka M

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

RESUMEN / SUMMARY: - Improving poor outcomes in patients with pancreatic cancer requires a greater understanding of the biological mechanisms contributing to radioresistance. We, therefore, sought to identify genes involved in the radioresistance of pancreatic cancer cells. Two pancreatic cancer cell lines, CFPAC-1 and Capan-1, were repeatedly exposed to radiation, establishing two radioresistant cell lines. Gene expression profiling using cDNA microarrays was performed to identify genes responsible for radioresistance. The levels of expression of mRNAs encoded by selected genes and their correlation with radiation dose resulting in 50% survival rate were analyzed in pancreatic cancer cell lines. The radiation dose resulting in a 50% survival rate was significantly higher in irradiated (IR) compared to parental CFPAC-1 cells (8.31+/-0.85 Gy vs. 2.14+/-0.04 Gy, P<0.0001), but was lower in IR compared with parental Capan-1 cells (2.66+/-0.24 Gy vs. 2.25+/-0.03Gy, P=0.04). cDNA microarray analysis identified 4 genes, including S100 calcium binding protein A4 (S100A4),

overexpressed and 23 genes underexpressed in the IR compared with the parental cell lines. The levels of S100A4 mRNA expression were correlated with radiation dose resulting in a 50% survival rate (Pearson's test, $R^2=0.81$, $P=0.0025$). S100A4 mRNA expression may predict radioresistance of pancreatic cancer cells and may play an important role in the poor response of pancreatic cancer cells to radiation therapy.

[85]

TÍTULO / TITLE: - MicroRNA-29^a induces resistance to gemcitabine through the Wnt/beta-catenin signaling pathway in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Int J Oncol. 2013 Oct;43(4):1066-72. doi: 10.3892/ijo.2013.2037. Epub 2013 Jul 24.

●● Enlace al texto completo (gratuito o de pago) [3892/ijo.2013.2037](#)

AUTORES / AUTHORS: - Nagano H; Tomimaru Y; Eguchi H; Hama N; Wada H; Kawamoto K; Kobayashi S; Mori M; Doki Y

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Graduate School of Medicine, Osaka University, Suita, Osaka 565-0871, Japan.

RESUMEN / SUMMARY: - Although we studied previously the mechanisms of resistance of pancreatic cancer cells to gemcitabine (GEM), prediction of the response to GEM remains unsatisfactory. The aim of this study was to investigate the relationship between miR-29^a expression and the response to GEM in pancreatic cancer cells. Changes in the growth-inhibitory effect of pancreatic cancer cells (MIAPaCa-2, PSN-1, BxPC-3 and Panc-1) to GEM were examined after overexpression or suppression of miR-29^a. We also examined the effect of miR-29^a on the Wnt/beta-catenin signaling pathway and investigated whether the altered growth-inhibitory effect by miR-29^a suppression was weakened after the addition of Wnt3a, a Wnt/beta-catenin signaling activator. MIAPaCa-2 and PSN-1 cells transfected with anti-miR-29^a showed significantly lower resistance to GEM. In the anti-miR-29^a-transfected cells, GEM induced significantly larger numbers of apoptotic cells and S phase accumulation compared to control cells, demonstrated by Annexin V assay and flow cytometric analysis of the cell cycle, respectively. The transfected cells showed overexpression of putative target molecules including Dkk1, Kremen2 and sFRP2 and lower activation of the Wnt/beta-catenin signaling pathway. The addition of Wnt3a weakened the augmented growth-inhibitory effect of anti-miR-29^a transfection. Our findings suggest that miR-29^a expression correlates significantly with the growth-inhibitory effect of GEM and that activation of the Wnt/beta-catenin signaling pathway mediated the miR-29^a-induced resistance to GEM in pancreatic cancer cell lines.

[86]

TÍTULO / TITLE: - Protease activated receptor-2 induces migration of pancreatic cancer cells in an extracellular ATP dependent manner.

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

REVISTA / JOURNAL: - J Thromb Haemost. 2013 Jul 31. doi: 10.1111/jth.12361.

●● Enlace al texto completo (gratis o de pago) [1111/jth.12361](#)

AUTORES / AUTHORS: - Shi K; Queiroz KC; Stap J; Richel DJ; Spek CA

INSTITUCIÓN / INSTITUTION: - Center for Experimental and Molecular Medicine, Academic Medical Center, Amsterdam, the Netherlands.

RESUMEN / SUMMARY: - BACKGROUND: Protease-activated receptor 2 (PAR-2) is a G protein-coupled receptor suggested to play an important role in proliferation and migration of tumor cells of epithelial origin. However, the role of PAR-2 in the setting of pancreatic cancer remains largely unexplored. OBJECTIVES: To understand the importance of PAR-2 in pancreatic cancer cell migration. METHODS AND RESULTS: The present study shows that PAR-2 does not affect pancreatic cancer cell proliferation but significantly induce migration of pancreatic cancer cells in scratch assays. Interestingly, PAR-2 does not affect migration in a trans-well setting. This apparent discrepancy depends on extracellular ATP release in the scratch assays, and addition of exogenous ATP induced PAR-2-dependent migration in trans-well assays, whereas a specific P2Y11 receptor antagonist prevents PAR-2 driven migration in scratch assays. In the scratch assays, inhibitors of Src, Rac, PKC, MEK, P38 and EGFR blocked PAR-2 driven migration whereas they did not affect FCS driven wound closure. CONCLUSION: Taken together, PAR-2 activation drives pancreatic cancer cell migration via an EGF-Src-Rac-p38/MEK/ERK1/2 signaling pathway, which is facilitated by extracellular ATP. Targeting the PAR-2/ATP driven signaling pathway may therefore limit cell migration, which could inhibit pancreatic cancer metastasis. This article is protected by copyright. All rights reserved.

[87]

TÍTULO / TITLE: - Molecular imaging in pancreatic cancer - A roadmap for therapeutic decisions.

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

REVISTA / JOURNAL: - Cancer Lett. 2013 Aug 11. pii: S0304-3835(13)00583-1. doi: 10.1016/j.canlet.2013.08.008.

●● Enlace al texto completo (gratis o de pago) [1016/j.canlet.2013.08.008](#)

AUTORES / AUTHORS: - Kramer-Marek G; Gore J; Korc M

INSTITUCIÓN / INSTITUTION: - Indiana University School of Medicine, Indianapolis, IN, USA.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is a deadly cancer characterized by multiple molecular alterations, the presence of an intense stroma, poor perfusion, and resistance to therapy. In addition to standard imaging techniques,

experimental imaging strategies, such as those utilizing molecular probes, nanoparticle-based agents, and tagged antibodies are actively being explored experimentally. It is hoped that advances in these technologies will allow for detecting PDAC at an early stage, and could serve to validate experimental therapies, rapidly identify non-responders, and assist in the design of novel therapeutic strategies tailored to the patient's molecular profile.

[88]

TÍTULO / TITLE: - Macrophages mediate gemcitabine resistance of pancreatic adenocarcinoma by upregulating cytidine deaminase.

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

REVISTA / JOURNAL: - Oncogene. 2013 Sep 2. doi: 10.1038/onc.2013.357.

●● Enlace al texto completo (gratis o de pago) [1038/onc.2013.357](#)

AUTORES / AUTHORS: - Weizman N; Krelin Y; Shabtay-Orbach A; Amit M; Binenbaum Y; Wong RJ; Gil Z

INSTITUCIÓN / INSTITUTION: - The Laboratory for Applied Cancer Research, Department of Otolaryngology Head and Neck Surgery, Rambam Medical Center, Haifa, Israel.

RESUMEN / SUMMARY: - Resistance to pharmacologic agents used in chemotherapy is common in most human carcinomas, including pancreatic ductal adenocarcinoma (PDA), which is resistant to almost all drugs, including gemcitabine, a nucleoside analog used as a first-line treatment. Poor survival rates of PDA patients have, therefore, not changed much over 4 decades. Recent data indicated that tumor-associated macrophages (TAMs), which are abundant in the microenvironment of several tumors, including PDA, secrete pro-tumorigenic factors that contribute to cancer progression and dissemination. In this study, we show for the first time that TAMs can also induce chemoresistance of PDA by reducing gemcitabine-induced apoptosis. Macrophages co-cultured with cancer cells or TAM-conditioned medium significantly reduced apoptosis and activation of the caspase-3 pathway during gemcitabine treatment. In vivo PDA models of mice, which have reduced macrophage recruitment and activation, demonstrated improved response to gemcitabine compared with controls. Similarly, inhibition of monocytes/macrophages trafficking by a CSF1-receptor antagonist GW2580 augmented the effect of gemcitabine in a transgenic mouse PDA model that was resistant to gemcitabine alone. Analysis of multiple proteins involved in gemcitabine delivery and metabolism revealed that TAMs induced upregulation of cytidine deaminase (CDA), the enzyme that metabolizes the drug following its transport into the cell. Decreasing CDA expression by PDA cells blocked the protective effect of TAMs against gemcitabine. These results provide the first evidence of a paracrine effect of TAMs, which mediates acquired resistance of cancer cells to chemotherapy. Modulation of macrophage trafficking or inhibition of CDA may offer a new strategy for augmenting the response of PDA to

chemotherapy.Oncogene advance online publication, 2 September 2013;
doi:10.1038/onc.2013.357.

[89]

TÍTULO / TITLE: - Mitochondrial phosphate transport during nutrient stimulation of INS-1E insulinoma cells.

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

REVISTA / JOURNAL: - Mol Cell Endocrinol. 2013 Aug 9;381(1-2):198-209. doi: 10.1016/j.mce.2013.08.003.

●● Enlace al texto completo (gratis o de pago) [1016/j.mce.2013.08.003](#)

AUTORES / AUTHORS: - Quan X; Das R; Xu S; Cline GW; Wiederkehr A; Wollheim CB; Park KS

INSTITUCIÓN / INSTITUTION: - Department of Physiology and Institute of Lifestyle Medicine, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea.

RESUMEN / SUMMARY: - Here, we have investigated the role of inorganic phosphate (Pi) transport in mitochondria of rat clonal beta-cells. In alpha-toxin-permeabilized INS-1E cells, succinate and glycerol-3-phosphate increased mitochondrial ATP release which depends on exogenous ADP and Pi. In the presence of substrates, addition of Pi caused mitochondrial matrix acidification and hyperpolarisation which promoted ATP export. Dissipation of the mitochondrial pH gradient or pharmacological inhibition of Pi transport blocked the effects of Pi on electrochemical gradient and ATP export. Knock-down of the phosphate transporter PiC, however, neither prevented Pi-induced mitochondrial activation nor glucose-induced insulin secretion. Using ³¹P NMR we observed reduction of Pi pools during nutrient stimulation of INS-1E cells. Interestingly, Pi loss was less pronounced in mitochondria than in the cytosol. We conclude that matrix alkalinisation is necessary to maintain a mitochondrial Pi pool, at levels sufficient to stimulate energy metabolism in insulin-secreting cells beyond its role as a substrate for ATP synthesis.

[90]

TÍTULO / TITLE: - Exercise as Medicine in the Management of Pancreatic Cancer: A Case Study.

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

REVISTA / JOURNAL: - Med Sci Sports Exerc. 2013 Sep 12.

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

[1249/MSS.0000000000000160](#)

AUTORES / AUTHORS: - Cormie P; Spry N; Jasas K; Johansson M; Yusoff IF; Newton RU; Galvao DA

INSTITUCIÓN / INSTITUTION: - 1Edith Cowan University Health and Wellness Institute, Edith Cowan University, Joondalup, Australia; 2 Department of Radiation Oncology, Sir Charles Gairdner Hospital, Nedlands, Australia; 3Faculty of Medicine, University of Western Australia, Australia; 4Department of Medical Oncology, Sir Charles Gairdner Hospital, Nedlands, Australia; 5Department of General Surgery, Sir Charles Gairdner Hospital, Nedlands, Australia; 6Department of Gastroenterology, Sir Charles Gairdner Hospital, Nedlands, Australia.

RESUMEN / SUMMARY: - Given the poor prognosis for patients diagnosed with pancreatic cancer, therapies that enhance the ability to tolerate adjuvant treatments, reduce the loss of physical functioning and optimize quality of life are critically important. Exercise may represent such a therapy however, no previous research has investigated the potential impact of exercise on outcomes in pancreatic cancer patients. **PURPOSE:** To determine the safety and efficacy of a 6-month supervised exercise program in a pancreatic cancer patient undergoing adjuvant treatment. **METHODS:** A case study was performed on a 49 year old male diagnosed with stage IIb pancreatic cancer. The patient had surgery (Whipple resection) followed by adjuvant chemotherapy (Gemcitabine and Fluorouracil) and radiotherapy (45 Gy). The patient initiated a supervised exercise program involving twice weekly resistance and aerobic exercise sessions during adjuvant therapy. Outcomes were assessed at baseline and following 3 and 6 months of exercise. **RESULTS:** The exercise program was well tolerated with 73% attendance throughout the 6 months. No treatment toxicities prevented the patient from complying with adjuvant treatment plans. Considerable improvements were observed at both 3- and 6-month assessment points for all measures of physical capacity and functional ability, lean mass, physical activity levels, general health and disease specific quality of life, cancer-related fatigue, sleep quality and psychological distress. **CONCLUSIONS:** In this first reported clinical case, exercise led to improvements in a variety of patient outcomes during adjuvant therapy for pancreatic cancer. This initial evidence has important clinical implications, indicating that exercise may be an effective adjunct therapy for the management of pancreatic cancer. Future trials are needed to confirm and expand our initial findings.

[91]

TÍTULO / TITLE: - Integration of Metabolomics and Transcriptomics Revealed a Fatty Acid Network Exerting Growth Inhibitory Effects in Human Pancreatic Cancer.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Sep 15;19(18):4983-4993. Epub 2013 Aug 5.

●● [Enlace al texto completo \(gratis o de pago\) 1158/1078-0432.CCR-13-0209](#)

AUTORES / AUTHORS: - Zhang G; He P; Tan H; Budhu A; Gaedcke J; Ghadimi BM; Ried T; Yfantis HG; Lee DH; Maitra A; Hanna N; Alexander HR; Hussain SP

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Pancreatic Cancer Unit, Laboratory of Human Carcinogenesis, Center for Cancer Research, Genetics Branch, National Cancer Institute, NIH, Bethesda; Pathology and Laboratory Medicine, Baltimore Veterans Affairs Medical Center, The Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins University School of Medicine, Division of Surgical Oncology, The Department of Surgery and the Marlene and Stewart Greenebaum Cancer Center, University of Maryland School of Medicine, Baltimore, Maryland; and Department of General and Visceral Surgery, University Medicine, Gottingen, Germany.

RESUMEN / SUMMARY: - **PURPOSE:** To identify metabolic pathways that are perturbed in pancreatic ductal adenocarcinoma (PDAC), we investigated gene-metabolite networks with integration of metabolomics and transcriptomics. **EXPERIMENTAL DESIGN:** We conducted global metabolite profiling analysis on two independent cohorts of resected PDAC cases to identify critical metabolites alteration that may contribute to the progression of pancreatic cancer. We then searched for gene surrogates that were significantly correlated with the key metabolites, by integrating metabolite and gene expression profiles. **RESULTS:** Fifty-five metabolites were consistently altered in tumors as compared with adjacent nontumor tissues in a test cohort (N = 33) and an independent validation cohort (N = 31). Weighted network analysis revealed a unique set of free fatty acids (FFA) that were highly coregulated and decreased in PDAC. Pathway analysis of 157 differentially expressed gene surrogates revealed a significantly altered lipid metabolism network, including key lipolytic enzymes PNLIP, CLPS, PNLIPRP1, and PNLIPRP2. Gene expressions of these lipases were significantly decreased in pancreatic tumors as compared with nontumor tissues, leading to reduced FFAs. More importantly, a lower gene expression of PNLIP in tumors was associated with poorer survival in two independent cohorts. We further showed that two saturated FFAs, palmitate and stearate, significantly induced TRAIL expression, triggered apoptosis, and inhibited proliferation in pancreatic cancer cells. **CONCLUSIONS:** Our results suggest that impairment in a lipolytic pathway involving lipases, and a unique set of FFAs, may play an important role in the development and progression of pancreatic cancer and provide potential targets for therapeutic intervention. Clin Cancer Res; 19(18); 4983-93. ©2013 AACR.

[92]

TÍTULO / TITLE: - Guggulsterone decreases proliferation and metastatic behavior of pancreatic cancer cells by modulating JAK/STAT and Src/FAK signaling.

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

REVISTA / JOURNAL: - Cancer Lett. 2013 Aug 3. pii: S0304-3835(13)00557-0. doi: 10.1016/j.canlet.2013.07.037.

●● Enlace al texto completo (gratis o de pago) 1016/j.canlet.2013.07.037

AUTORES / AUTHORS: - Macha MA; Rachagani S; Gupta S; Pai P; Ponnusamy MP; Batra SK; Jain M

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, NE 68198-5870, USA.

RESUMEN / SUMMARY: - Inadequate efficacy, high toxicity and drug resistance associated with existing chemotherapeutic agents mandate a need for novel therapeutic strategies for highly aggressive Pancreatic Cancer (PC). Guggulsterone (GS) exhibits potent anti-proliferative effects against various cancer cells and has emerged as an attractive candidate for use in complementary or preventive cancer therapies. However, the knowledge regarding the therapeutic potential of GS in PC is still limited and needs to be explored. We studied the effect of GS on PC cell growth, motility and invasion and elucidated the molecular mechanisms associated with its anti-tumor effects. Treatment of Capan1 and CD18/HPAF PC cells with GS resulted in dose- and time-dependent growth inhibition and decreased colony formation. Further, GS treatment induced apoptosis and cell cycle arrest as assessed by Annexin-V assay and FACS analysis. Increased apoptosis following GS treatment was accompanied with Bad dephosphorylation and its translocation to the mitochondria, increased Caspase-3 activation, decreased Cyclin D1, Bcl-2 and XIAP expression. Additionally, GS treatment decreased motility and invasion of PC cells by disrupting cytoskeletal organization, inhibiting activation of FAK and Src signaling and decreased MMP9 expression. More importantly, GS treatment decreased mucin MUC4 expression in Capan1 and CD18/HPAF cells through transcriptional regulation by inhibiting Jak/STAT pathway. In conclusion, our results support the utility of GS as a potential therapeutic agent for lethal PC.

[93]

TÍTULO / TITLE: - Observational study of natural history of small sporadic non-functioning pancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - J Clin Endocrinol Metab. 2013 Sep 20.

●● Enlace al texto completo (gratis o de pago) [1210/jc.2013-2604](#)

AUTORES / AUTHORS: - Gaujoux S; Partelli S; Maire F; D'Onofrio M; Larroque B; Tamburrino D; Sauvanet A; Falconi M; Ruzniewski P

INSTITUCIÓN / INSTITUTION: - 1Department of HPB Surgery - PMAD - Hopital Beaujon - AP-HP - Clichy, France.

RESUMEN / SUMMARY: - Context:Asymptomatic sporadic non-functioning well-differentiated pancreatic neuroendocrine tumors (NF-PNET) are increasingly diagnosed, and their management is controversial because of their overall good but heterogeneous prognosis.Objective:To assess the natural history of asymptomatic

sporadic NF-PNETs smaller than 2 cm in size and the risk-benefit balance of non-operative management. Experimental design: From January 2000 to June 2011, 46 patients with proven AS-NF-PNET smaller than 2 cm in size were followed-up for at least 18 months with serial imaging in tertiary referral centers. Results: Patients were mainly female (65%), with a median age of 60 years. Tumors were mainly located in the pancreatic head (52%), with a median lesion size of 13 mm (9-15). After a median follow-up of 34 months (24-52) and an average of 4 (3-6) serial imaging sessions, distant or nodal metastases appeared on the imaging in none of the patients. In 6 (13%) patients, a $\geq 20\%$ increase in size was observed. Overall median tumor growth was 0.12 mm per year and neither patients nor tumor characteristics were found to be significant predictors of tumor growth. Overall, 8 patients (17%) underwent surgery after a median time from initial evaluation of 41 months (27-58); all resected lesions were ENETS T stage 1 (n=7) or 2 (n=1), grade 1, node negative, with neither vascular nor peripancreatic fat invasion. Conclusions: In selected patients, non-operative management of asymptomatic sporadic NF-PNET smaller than 2 cm in size is safe. Larger and prospective multicentric studies with long-term follow-up are now needed to validate this "wait and see" policy.

[94]

TÍTULO / TITLE: - The neurotrophic factor neurturin contributes towards an aggressive cancer cell phenotype, neuropathic pain and neuronal plasticity in pancreatic cancer.

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

REVISTA / JOURNAL: - Carcinogenesis. 2013 Sep 25.

●● [Enlace al texto completo \(gratis o de pago\) 1093/carcin/bgt312](#)

AUTORES / AUTHORS: - Wang K; Demir IE; D'Haese JG; Tieftrunk E; Kujundzic K; Schorn S; Xing B; Kehl T; Friess H; Ceyhan GO

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Klinikum rechts der Isar, Technische Universität München, Munich, Germany.

RESUMEN / SUMMARY: - Neurotrophic factors possess an emerging role in the pathophysiology of several gastrointestinal disorders, regulating innervation, pain sensation and disease-associated neuroplasticity. Here, we aimed at characterizing the role of the neurotrophic factor neurturin (NRTN) and its receptor GFRalpha-2 in pancreatic cancer (PCa) and pancreatic neuropathy. For this purpose, NRTN and GFRalpha-2 were studied in normal human pancreas (NP) and PCa tissues via immunohistochemistry, QRT-PCR, immunoblotting and correlated to abdominal pain. The impact of NRTN/GFRalpha-2 on PCa cell (PCC) biology was investigated via exposure to hypoxia, MTT viability and Matrigel invasion assays in native and specific siRNA-silenced PCCs. To assess the influence of NRTN on pancreatic neuroplasticity and neural invasion (NI), its impact was explored via an in vitro "neuroplasticity assay" and a 3D-neural-migration-assay. NRTN and GFRalpha-2 demonstrated a site-specific

upregulation in PCa, predominantly in nerves, PCCs and extracellular matrix. Patients with severe pain demonstrated higher intraneural GFRalpha-2-immunoreactivity than patients with no pain. PCa tissue and PCCs contained increased amounts of NRTN, which was suppressed under hypoxia. NRTN promoted PCC invasiveness, and silencing of NRTN limited both PCC proliferation and invasion. Depletion of NRTN from PCa tissue extracts and PCC supernatants decreased axonal sprouting in neuronal cultures, but did not influence glial density. Silencing of NRTN in PCCs boosted NI. We conclude that increased NRTN/GFRalpha-2 in PCa seems to promote an aggressive PCC phenotype and neuroplasticity in PCa. Accelerated NI following NRTN suppression constitutes a novel explanation for the attraction of PCC to nerves in the hypoxic PCa tumor microenvironment.

[95]

TÍTULO / TITLE: - Phase II study of pazopanib monotherapy in metastatic gastroenteropancreatic neuroendocrine tumours.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Sep 17;109(6):1414-9. doi: 10.1038/bjc.2013.470. Epub 2013 Aug 29.

●● Enlace al texto completo (gratis o de pago) [1038/bjc.2013.470](#)

AUTORES / AUTHORS: - Ahn HK; Choi JY; Kim KM; Kim H; Choi SH; Park SH; Park JO; Lim HY; Kang WK; Lee J; Park YS

INSTITUCIÓN / INSTITUTION: - 1] Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea [2] Department of Internal Medicine, Gachon University Gil Medical Center, Incheon, Korea.

RESUMEN / SUMMARY: - Background:Treatment options for patients with metastatic gastroenteropancreatic neuroendocrine tumours (GEP NETs) are still limited. We investigated the antitumour activity and safety profile of pazopanib - a multitarget drug with anti-angiogenic activity in patients with metastatic GEP NETs.Methods:This was a nonrandomised, open-labeled, single-center phase II study. Pazopanib was orally administered at a dose of 800 mg daily continuously with a 28-day cycle. The primary end point was an objective response rate according to Response Evaluation Criteria in Solid Tumors (RECIST). The secondary end points were progression-free survival (PFS), overall survival (OS) and safety. An independent review of objective response was planned. The trial is registered with ClinicalTrials.gov, NCT number 01099540. Correlative biomarker analyses were performed.Results:Between April 2010 and February 2012, a total of 37 patients were enrolled. Thirty-two percent of the enrolled patients had pancreatic primary and 22% of the patients had colorectal primary NETs. This phase II study demonstrated an objective response rate of 18.9% (7 of the 37, 95% CI 8.0-35.2) and a disease control rate (CR+confirmed PR+stable

disease) of 75.7% (28 of the 37, 95% CI, 58.8-88.2) in metastatic GEP NETs. The independent review demonstrated a higher overall response rate of 24.3% (95% CI, 11.8-41.2%) with nine confirmed PRs. Conclusion: Pazopanib showed a comparable efficacy to other targeted agents not only in pancreatic NETs but also in NETs originating from gastrointestinal (GI) tract.

[96]

TÍTULO / TITLE: - HIF1 Contributes to Hypoxia-Induced Pancreatic Cancer Cells Invasion via Promoting QSOX1 Expression.

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

REVISTA / JOURNAL: - Cell Physiol Biochem. 2013;32(3):561-568. Epub 2013 Aug 30.

●● Enlace al texto completo (gratis o de pago) [1159/000354460](#)

AUTORES / AUTHORS: - Shi CY; Fan Y; Liu B; Lou WH

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Zhongshan Hospital, Fudan University, 136 Yi Xue Yuan Road, Shanghai, China.

RESUMEN / SUMMARY: - Background: Quiescin sulfhydryl oxidase 1 (QSOX1), which oxidizes sulfhydryl groups to form disulfide bonds in proteins, is found to be over-expressed in various pancreatic cancer cell lines and patients. QSOX1 promotes invasion of pancreatic cancer cells by activating MMP-2 and MMP-9. However, its regulatory mechanism remains largely undefined. Methods: Real-time PCR and Western blot were employed to detect the expression of QSOX1 in human pancreatic cancer cell lines under hypoxic condition. Luciferase reporter and CHIP assays were used to assess the regulation of QSOX1 by hypoxia-inducible factor 1 (HIF-1). Small interfering RNA (siRNA) was applied to knock down endogenous expression of QSOX1. Matrigel-coated invasion chamber essays were conducted to detect the invasion capacity of QSOX1-depleted cells. Results: Both hypoxia and hypoxia mimicking reagent up-regulated the expression of QSOX1 in human pancreatic cancer cell lines. Knockdown of HIF-1alpha eliminated hypoxia induced QSOX1 expression. HIF-1alpha was found directly bound to two hypoxia-response elements (HRE) of QSOX1 gene, both of which were required for HIF-1 induced QSOX1 expression. Moreover, QSOX1 silencing blocked hypoxia-induced pancreatic cancer cells invasion. Conclusion: QSOX1 is a direct target of HIF-1 and may contribute to hypoxia-induced pancreatic cancer cells invasion. © 2013 S. Karger AG, Basel.

[97]

TÍTULO / TITLE: - Trisomy of the Dscr1 gene suppresses early progression of pancreatic intraepithelial neoplasia driven by oncogenic Kras.

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

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Sep 13. pii: S0006-291X(13)01504-0. doi: 10.1016/j.bbrc.2013.09.033.

●● Enlace al texto completo (gratis o de pago) 1016/j.bbrc.2013.09.033

AUTORES / AUTHORS: - Lee JC; Shin J; Baek KH

INSTITUCIÓN / INSTITUTION: - Department of Molecular and Cellular Biology, Samsung Biomedical Research Institute, Sungkyunkwan University School of Medicine, Suwon, Gyeonggi 440-746, Republic of Korea.

RESUMEN / SUMMARY: - Individuals with Down syndrome exhibit remarkably reduced incidence of most solid tumors including pancreatic cancer. Multiple mechanisms arising from the genetic complexity underlying Down syndrome has been suggested to contribute to such a broad cancer protection. In this study, utilizing a genetically engineered mouse model of pancreatic cancer, we demonstrate that trisomy of the Down syndrome critical region-1 (Dscr1), an endogenous calcineurin inhibitor localized on chromosome 21, suppresses the progression of pancreatic intraepithelial neoplasia-1^a (PanIN-1^a) to PanIN-1B lesions without affecting the initiation of PanIN lesions mediated by oncogenic KrasG12D. In addition, we show that Dscr1 trisomy attenuates nuclear localization of nuclear factor of activated T-cells (NFAT) accompanied by upregulation of the p15Ink4b tumor suppressor and reduction of cell proliferation in early PanIN lesions. Our data suggest that attenuation of calcineurin-NFAT signaling in neoplastic pancreatic ductal epithelium by a single extra copy of Dscr1 is sufficient to inhibit the progression of early PanIN lesions driven by oncogenic Kras, and thus may be a potential mechanism underlying reduced incidence of pancreatic cancer in Down syndrome individuals.

[98]

TÍTULO / TITLE: - Identification of genes and candidate agents associated with pancreatic cancer.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Aug 10.

●● Enlace al texto completo (gratis o de pago) 1007/s13277-013-1009-3

AUTORES / AUTHORS: - Wang BS; Liu Z; Sun SL; Zhao Y

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Shengjing Hospital of China Medical University, Shenyang, 110004, China, wangbaosheng@hotmail.com.

RESUMEN / SUMMARY: - Pancreatic cancer is a malignant neoplasm originating from transformed cells arising in tissues forming the pancreas. A major challenge in current cancer research is biological interpretation of complexity of cancer somatic mutation profiles. It has been suggested that several molecular alterations may play important roles in pancreatic carcinogenesis. In this study, by using the GSE28735 affymetrix microarray data accessible from Gene Expression Omnibus (GEO) database, we identified differentially expressed genes (DEGs) between paired pancreatic cancer

tissues and adjacent nontumor tissues, followed the protein-protein interaction of the DEGs. Our study identified thousands of DEGs involved in regulation of cell cycle and apoptosis in progression of pancreatic cancer. Sp1 was predicted to be the major regulator by transcription factors analysis. From the protein-protein interaction networks, we found that Tk1 might play an important role in the progression of pancreatic cancer. Finally, we predicted candidate agents, including tomatidine and nialamide, which may be used as drugs to treat pancreatic cancer. In conclusion, our data provide a comprehensive bioinformatics analysis of genes and pathways which may be involved in the progression of pancreatic cancer.

[99]

TÍTULO / TITLE: - Teres hepatis ligament flap plasty to prevent pancreatic fistula after tumor enucleation.

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

REVISTA / JOURNAL: - J Am Coll Surg. 2013 Oct;217(4):e29-34. doi: 10.1016/j.jamcollsurg.2013.06.014.

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

[1016/j.jamcollsurg.2013.06.014](#)

AUTORES / AUTHORS: - Hackert T; Lozanovski VJ; Werner J; Buchler MW; Schemmer P

INSTITUCIÓN / INSTITUTION: - Department of General and Transplant Surgery, University Hospital of Heidelberg, Heidelberg, Germany.

[100]

TÍTULO / TITLE: - Cell Surface Sialic Acid Modulates Extracellular Matrix Adhesion and Migration in Pancreatic Adenocarcinoma Cells.

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

REVISTA / JOURNAL: - Pancreas. 2013 Aug 5.

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

[1097/MPA.0b013e31829d9090](#)

AUTORES / AUTHORS: - Bassaganas S; Perez-Garay M; Peracaula R

INSTITUCIÓN / INSTITUTION: - From the Department of Biology, University of Girona, Girona, España.

RESUMEN / SUMMARY: - OBJECTIVES: Tumor cells modulate their extracellular matrix (ECM) adhesion and migration to become more metastatic. Moreover, they show an increase in sialic acid, which could have an effect on their ECM adhesion and migration. This work describes the influence of pancreatic adenocarcinoma cell surface alpha2,3- and alpha2,6-sialic acid determinants on the aforementioned processes. METHODS: We have characterized the cell surface alpha2,3- and alpha2,6-sialic acids, and sialyl-Lewis x levels and the integrin levels of 2 pancreatic adenocarcinoma cell

lines, Capan-1 and MDAPanc-28, grown at different cell densities, and also of the ST3Gal III overexpressing Capan-1 cells, C31. We have measured their adhesion to several ECM proteins and their migration through collagen with and without blocking their sialic acid determinants. RESULTS: Adhesion to ECM proteins of Capan-1 and MDAPanc-28 grown at different cell densities, and of C31, depended on their cell surface sialic acid determinants repertoire, correlating the higher alpha2,6-sialic acid levels with their increased ECM adhesion. Cell migration also depended on their sialic acid determinants expression; and in this case, higher alpha2,3-sialic acid levels correlated with a more migratory phenotype. CONCLUSION: This study shows how the intrinsic heterogeneity of cell membrane sialylation regulates the adhesive and migratory potential of pancreatic adenocarcinoma cells.

[101]

TÍTULO / TITLE: - Splenic Abscess Caused by Streptococcus gallolyticus Subspecies pasteurianus as Presentation of A Pancreatic Cancer: A Case Report and A Brief Review.

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

REVISTA / JOURNAL: - J Clin Microbiol. 2013 Sep 11.

●● Enlace al texto completo (gratis o de pago) [1128/JCM.01709-13](#)

AUTORES / AUTHORS: - Su Y; Miao B; Wang H; Wang C; Zhang S

INSTITUCIÓN / INSTITUTION: - Department of Infection and Critical Care Medicine, Beijing Friendship Hospital, Capital University of Medical Sciences, Beijing 100050, China.

RESUMEN / SUMMARY: - Splenic abscess caused by Streptococcus bovis are rarely reported in the literature and are mainly seen in patients with endocarditis and associated colonic neoplasia/carcinoma. We report the first case of splenic abscess caused by Streptococcus gallolyticus subspecies pasteurianus (S. bovis biotype II/2) as presentation of a pancreatic cancer.

[102]

TÍTULO / TITLE: - Claudin 18.2 is a target for IMAB362 antibody in pancreatic neoplasms.

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

REVISTA / JOURNAL: - Int J Cancer. 2013 Jul 30. doi: 10.1002/ijc.28400.

●● Enlace al texto completo (gratis o de pago) [1002/ijc.28400](#)

AUTORES / AUTHORS: - Woll S; Schlitter AM; Dhaene K; Roller M; Esposito I; Sahin U; Tureci O

INSTITUCIÓN / INSTITUTION: - Ganymed Pharmaceuticals AG, Mainz, Germany.

RESUMEN / SUMMARY: - The majority of pancreatic neoplasms are characterized by a generally lethal progress within a short period of time after primary diagnosis and the mortality of patients is expected to increase further. Due to lack of efficient screening

programs and moderate response to treatments, novel compounds for treatment are needed. We investigated the CLDN18.2 expression in affected patients as in vitro feasibility study for a potential treatment with the novel antibody IMAB362. Therefore we analyzed the expression of CLDN18.2 in normal pancreatic tissues (N=24), primary lesions (N=202), metastases (N=84) and intra-individually matched samples (N=48) of patients with PDAC, NEN and acinar cell carcinoma. A standardized method for evaluation by immunohistochemistry was developed. The specific staining was evaluated by two independent raters and analysis of staining intensities (range 0-3+) and relative proportions of tumor cells were performed. 103 (59.2%) samples of primary PDAC were found positive. The vast majority of positive samples were characterized to highly express CLDN18.2: 54.6% (N=95) with staining intensities of $\geq 2+$. NEN were positive in 20% of cases (all $\geq 2+$). Metastases of pancreatic neoplasms were also frequently found positive with comparable high rates (69.4% of lymph node and 65.7% of liver metastases). The rate of CLDN18.2 positivity is high in pancreatic neoplasms whereby the expression is not limited to the primaries but is also maintained upon metastasis. Thus a considerable number of patients with pancreatic neoplasms would be in principle eligible for a CLDN18.2-targeting approach.

[103]

TÍTULO / TITLE: - The winning FORMULA-tion: the development of paclitaxel in pancreatic cancer.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Aug 5.

●● [Enlace al texto completo \(gratis o de pago\) 1158/1078-0432.CCR-13-1356](#)

AUTORES / AUTHORS: - Ma WW; Hidalgo M

INSTITUCIÓN / INSTITUTION: - Medicine, Roswell Park Cancer Institute.

RESUMEN / SUMMARY: - Paclitaxel has wide application in anti-cancer therapy but was never considered an efficacious agent in pancreatic cancer. A review of the experience with the Cremaphor (Cre) formulation hinted paclitaxel's activity in pancreatic cancer but the early development was hampered by significant toxicities such as neutropenia and infection at clinically tolerable doses. However, such efficacy was confirmed in the recently completed phase III MPACT trial where the addition of nab-paclitaxel to gemcitabine significantly improved the survival of metastatic pancreatic cancer patients. Several other Cremaphor-free formulations of paclitaxel had also been evaluated in pancreatic cancer and the reasons for the success of the albumin nanoparticulate are examined here. In the era of biological and molecularly-targeted agents, the success of nab-paclitaxel in the recalcitrant pancreatic cancer is a timely reminder of the importance and relevance of pharmacology and novel drug delivery technology in the development of anti-cancer drugs.

[104]

TÍTULO / TITLE: - A Tumorigenic Factor Interactome Connected Through Tumor Suppressor MicroRNA-198 in Human Pancreatic Cancer.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Aug 29.

●● Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-12-3776](#)

AUTORES / AUTHORS: - Marin-Muller C; Li D; Bharadwaj U; Li M; Chen C; Hodges S; Fisher W; Mo Q; Hung MC; Yao Q

INSTITUCIÓN / INSTITUTION: - Michael E. DeBakey Department of Surgery, Suite O200, Baylor College of Medicine.

RESUMEN / SUMMARY: - **PURPOSE:** The majority of pancreatic cancers (PCs) overexpress mesothelin (MSLN), which contributes to enhanced proliferation, invasion and migration. However, the MSLN regulatory network is still unclear. Here, we investigated the regulation of a panel of tumorigenic factors, and explored the potential of MSLN regulated miR-198 treatment in vivo. **EXPERIMENTAL DESIGN:** The expression and functional regulation of the tumorigenic factors MSLN, NF-kappaB, and the homeobox transcription factors (TFs) POU2F2 (OCT-2), Pre-B-cell leukemia homeobox factor 1 (PBX-1), valosin-containing protein (VCP), and miR-198 were studied in PC cell lines, patient tumor samples and in xenograft PC mouse models. **RESULTS:** We found that miR-198 is downregulated in PC and is involved in an intricate reciprocal regulatory loop with MSLN, which represses miR-198 through NF-kappaB-mediated OCT-2 induction. Furthermore, miR-198 repression leads to overexpression of PBX-1 and VCP. The dysregulated PBX-1/VCP axis leads to increased tumorigenicity. Reconstitution of miR-198 in PC cells results in reduced tumor growth, metastasis, and increased survival through direct targeting MSLN, PBX-1, and VCP. Most interestingly, reduced levels of miR-198 in human tissue samples are associated with upregulation of these tumorigenic factors (MSLN, OCT-2, PBX-1, VCP) and predict poor survival. Reduced miR-198 expression links this tumor network signature and prognosticates poor patient outcome. High miR-198 disrupts the network and predicts better prognosis and increased survival. **CONCLUSIONS:** MiR-198 acts as a central tumor suppressor and modulates the molecular makeup of a critical interactome in PC, indicating a potential prognostic marker signature and the therapeutic potential of attacking this tumorigenic network through a central vantage point.

[105]

TÍTULO / TITLE: - Propofol induces apoptosis and increases gemcitabine sensitivity in pancreatic cancer cells in vitro by inhibition of nuclear factor-kappaB activity.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Sep 7;19(33):5485-92. doi: 10.3748/wjg.v19.i33.5485.

●● Enlace al texto completo (gratis o de pago) [3748/wjg.v19.i33.5485](https://doi.org/10.3748/wjg.v19.i33.5485)

AUTORES / AUTHORS: - Du QH; Xu YB; Zhang MY; Yun P; He CY

INSTITUCIÓN / INSTITUTION: - Qi-Hang Du, Yan-Bing Xu, Meng-Yuan Zhang, Peng Yun, Chang-Yao He, Department of Anesthesiology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan 250021, Shandong Province, China.

RESUMEN / SUMMARY: - AIM: To investigate the effect of propofol on human pancreatic cells and the molecular mechanism of propofol action. METHODS: We used the human pancreatic cancer cell line MIAPaCa-2 for in vitro studies measuring growth inhibition and degree of apoptotic cell death induced by propofol alone, gemcitabine alone, or propofol followed by gemcitabine. All experiments were conducted in triplicate and carried out on three or more separate occasions. Data were means of the three or more independent experiments +/- SE. Statistically significant differences were determined by two-tailed unpaired Student's t test and defined as P < 0.05. RESULTS: Pretreatment of cells with propofol for 24 h followed by gemcitabine resulted in 24%-75% growth inhibition compared with 6%-18% when gemcitabine was used alone. Overall growth inhibition was directly correlated with apoptotic cell death. We also showed that propofol potentiated gemcitabine-induced killing by downregulation of nuclear factor-kappaB (NF-kappaB). In contrast, NF-kappaB was upregulated when pancreatic cancer cells were exposed to gemcitabine alone, suggesting a potential mechanism of acquired chemoresistance. CONCLUSION: Inactivation of the NF-kappaB signaling pathway by propofol might abrogate gemcitabine-induced activation of NF-kappaB, resulting in chemosensitization of pancreatic tumors to gemcitabine.

[106]

TÍTULO / TITLE: - Performance Status Is An Important Prognostic Factor In Second Line Treatment of Pancreaticobiliary Adenocarcinoma.

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

REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Aug 9;60(126):1479-1483. doi: 10.5754/hge13269.

●● Enlace al texto completo (gratis o de pago) [5754/hge13269](https://doi.org/10.5754/hge13269)

AUTORES / AUTHORS: - Erdogan B; Turmen E; Uzunoglu S; Tanr U0131verdi O; Cicin I

RESUMEN / SUMMARY: - Background/Aims: To define the factors related with disease control and survival in patients with pancreaticobiliary adenocarcinoma treated with second-line therapy. Methodology: We retrospectively reviewed the data of 39 pancreaticobiliary adenocarcinoma patients treated with second-line chemotherapy between 2000 and 2012. Age, gender, origin of tumor, location of tumor, stage at diagnosis, Eastern Cooperative Oncology Group (ECOG) performance status, progression site, progression free survival (PFS) for first-line therapy, disease control at

first-line therapy and chemotherapy protocols are analyzed for disease control rate, PFS and overall survival (OS). Results: Disease control was recorded in 21 (53.8%) patients (20 stable disease, 1 partial response). Disease control rate was higher in patients with good performance status ($p = 0.03$). Disease control at first-line therapy was not a predictor of disease control at second-line ($p = 0.6$). Response to first-line therapy and other prognostic factors was not related with disease control. Progression free survival and OS was significantly longer in patients with good ECOG performance status (0-1) ($p = 0.01$, $p = 0.006$). Choice of chemotherapy (single agent or combination) and other factors did not have any impact on PFS and OS. In multivariate analysis; disease control was independent prognostic factor for both PFS and OS ($p < 0.001$), ($p < 0.001$). Conclusions: Disease control and performance status are two important prognostic factors. Chemotherapy regimen has no impact on disease control and survival. Salvage chemotherapy can be considered for patients with good performance status whether they are resistant to first-line therapy or not.

[107]

TÍTULO / TITLE: - Combination treatment with comprehensive cryoablation and immunotherapy in metastatic pancreatic cancer.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1143-9. doi: 10.1097/MPA.0b013e3182965dde.

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

[1097/MPA.0b013e3182965dde](#)

AUTORES / AUTHORS: - Niu L; Chen J; He L; Liao M; Yuan Y; Zeng J; Li J; Zuo J; Xu K

INSTITUCIÓN / INSTITUTION: - From the *Fuda Cancer Hospital, School of Medicine, Jinan University; daggerFuda Institute of Cryosurgery for Cancer; and double daggerFuda Hospital, School of Medicine, Jinan University, Guangzhou, China.

RESUMEN / SUMMARY: - **OBJECTIVE:** The aim of this study was to retrospectively assess the effect of comprehensive cryosurgery (ablation of intrapancreatic and extrapancreatic tumors) plus immunotherapy in metastatic pancreatic cancer.

METHODS: We divided 106 patients (57 men, 49 women; median age, 65 years) into the cryoimmunotherapy (31 patients), cryotherapy (36 patients), immunotherapy (17 patients), and chemotherapy groups (22 patients). Pretreatment immune function was tested in patients who underwent immunotherapy. Overall survival (OS) after diagnosis of metastatic pancreatic cancer was assessed after a 4-year follow-up.

RESULTS: Median OS was higher in the cryoimmunotherapy (13 months) and cryotherapy groups (7 months) than in the chemotherapy group (3.5 months; both $P < 0.001$) and was higher in the cryoimmunotherapy group than in the cryotherapy ($P < 0.05$) and immunotherapy groups (5 months; $P < 0.001$). In both the cryoimmunotherapy and cryotherapy groups, median OS was higher after multiple

cryoablations than after a single cryoablation ($P = 0.0048$ and 0.041 , respectively). In both groups, the median OS was higher in patients with normal immunologic function than in those with immune dysfunction ($P < 0.0001$ and $P = 0.0004$, respectively). CONCLUSIONS: Cryoimmunotherapy significantly increased OS in metastatic pancreatic cancer. Multiple cryoablations and normal pretreatment immunologic function were associated with better prognosis.

[108]

TÍTULO / TITLE: - Intraductal Papillary Mucinous Neoplasms With Associated Invasive Carcinoma of the Pancreas: Imaging Findings and Diagnostic Performance of MDCT for Prediction of Prognostic Factors.

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

REVISTA / JOURNAL: - AJR Am J Roentgenol. 2013 Sep;201(3):565-72. doi: 10.2214/AJR.12.9511.

●● Enlace al texto completo (gratis o de pago) [2214/AJR.12.9511](#)

AUTORES / AUTHORS: - Kim JH; Eun HW; Kim KW; Lee JY; Lee JM; Han JK; Choi BI

INSTITUCIÓN / INSTITUTION: - 1 Department of Radiology and Institute of Radiation Medicine, Seoul National University College of Medicine, 101 Daehang-no, Chongno-gu, Seoul 110-744, Korea.

RESUMEN / SUMMARY: - OBJECTIVE. The purpose of this study was to assess the diagnostic accuracy of MDCT for determining the prognostic factors, including the T category, lymph node metastasis, tumor size, and perineural invasion, in surgically proven intraductal papillary mucinous neoplasms (IPMNs) with an associated invasive carcinoma (IPMC) and to investigate the imaging findings. MATERIALS AND METHODS. Our study group consisted of 38 patients with surgically proven IPMC who underwent preoperative dynamic CT. Two radiologists retrospectively assessed the morphologic type of IPMN, size of the cyst, size of the main pancreatic duct, and presence or absence of mural nodules. The radiologists also assessed the T category, lymph node metastasis, and perineural invasion. They graded the perineural invasion using a 3-point scale as follows: 1, normal; 2, streaky and strandlike structure in fat tissue as well as a fine, reticular pattern; and 3, irregular masses adjacent to the lesions. Statistical analyses were performed using receiver operating characteristic analysis, the McNemar test, and Fisher exact test. Kappa statistics were used to determine interobserver agreement. RESULTS. The morphologic types of IPMC included the main-duct type ($n = 11$, 29%), combined type ($n = 18$, 47%), and branch-duct type ($n = 9$, 24%). The diagnostic accuracy for the T category was 73.7% ($n = 28$) and 68.4% ($n = 26$) and for the lymph node metastasis was 68.4% ($n = 26$) and 76.3% ($n = 29$), respectively, for the two readers, with moderate interobserver agreement ($\kappa = 0.636$ and 0.708). The areas under the receiver operating characteristic curve for perineural invasion were 0.868 and 0.821. The sensitivity, specificity, and positive predictive value

were 100%, 71.4%, 55.5%, and 90%, 71.4%, 52.9%, respectively. Interobserver agreement was moderate ($\kappa = 0.659$). The tumor size seen on CT was not statistically different from the tumor size determined on pathology ($3.9 \pm [SD] 2.7$ cm vs 3.8 ± 2.1 cm, $p = 0.582$). The main duct size was 11.5 ± 6.2 mm. Mural nodules were detected in 74% ($n = 28$) of our study patients. CONCLUSION. CT might be useful for preoperatively evaluating the T category, lymph node metastasis, tumor size, and perineural invasion of IPMC. Main pancreatic duct dilatation and the presence of mural nodules are common findings of IPMC.

[109]

TÍTULO / TITLE: - Extracts from *Leonurus sibiricus* L. increase insulin secretion and proliferation of rat INS-1E insulinoma cells.

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

REVISTA / JOURNAL: - J Ethnopharmacol. 2013 Aug 24. pii: S0378-8741(13)00555-2. doi: 10.1016/j.jep.2013.08.013.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.jep.2013.08.013](#)

AUTORES / AUTHORS: - Schmidt S; Jakab M; Jav S; Streif D; Pitschmann A; Zehl M; Purevsuren S; Glasl S; Ritter M

INSTITUCIÓN / INSTITUTION: - Institute of Physiology and Pathophysiology, Paracelsus Medical University Salzburg, 5020 Salzburg, Austria. Electronic address: sabine.schmidt@pmu.ac.at.

RESUMEN / SUMMARY: - ETHNOPHARMACOLOGICAL RELEVANCE: Traditional Mongolian medicine (TMM) uses preparations from herbs as one form of medication for the treatment of a diversity of diseases including diabetes mellitus (DM). We evaluated the effect of extracts from the plant *Leonurus sibiricus* L. (LS), used in TMM to treat typical symptoms of type 2 DM, on insulin secretion, electrophysiological properties, intracellular calcium concentration and cell proliferation of INS-1E insulinoma cells under standard cell culture conditions (SCC; 11.1mM glucose). MATERIALS AND METHODS: Insulin secretion was measured by ELISA, electrical properties were assessed by whole cell patch clamping, intracellular calcium concentration (Cai) by Fluo-4 time lapse imaging, insulin receptor expression was verified by RT-PCR and cell proliferation assessed by CellTiter-Glo® cell viability assay. RESULTS: Insulin released from INS-1E cells into the culture medium over 24h was significantly increased in presence of 500mg/L aqueous LS extract (LS OWE) as well as methanolic LS extract (LS MeOH/H₂O) but not in the presence of the butanol-soluble extract (LS MeOH/BuOH). Acute application of LS OWE resulted in a depolarization of the cell membrane potential paralleled by an initial increase and subsequent decline and silencing of action potential frequency, by KATP channel inhibition, persisting depolarization and an increase in Cai. The electrophysiological effects were comparable to those of 100µM tolbutamide, which, however failed to elevate insulin secretion under SCC.

Furthermore all LS extracts stimulated INS-1E cell proliferation. CONCLUSIONS: The finding that extracts from Leonurus sibiricus L. enhance insulin secretion and/or foster cell proliferation may provide possible explanations for the underlying therapeutic principles in the empirical use of LS-containing formulations in DM and DM-related disorders as applied in TMM.

[110]

TÍTULO / TITLE: - Diffusion-weighted MRI monitoring of pancreatic cancer response to radiofrequency heat-enhanced intratumor chemotherapy.

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

REVISTA / JOURNAL: - NMR Biomed. 2013 Sep 4. doi: 10.1002/nbm.3014.

●● [Enlace al texto completo \(gratis o de pago\) 1002/nbm.3014](#)

AUTORES / AUTHORS: - Zhang T; Zhang F; Meng Y; Wang H; Le T; Wei B; Lee D; Willis P; Shen B; Yang X

INSTITUCIÓN / INSTITUTION: - Image-Guided Bio-Molecular Intervention Research and Section of Vascular and Interventional Radiology, Department of Radiology, University of Washington School of Medicine, Seattle, WA, USA; Department of Radiology, Haerbin Medical University Affiliated 4th Hospital, Haerbin, China.

RESUMEN / SUMMARY: - The aim of this study was to evaluate the feasibility of using diffusion-weighted MRI to monitor the early response of pancreatic cancers to radiofrequency heat (RFH)-enhanced chemotherapy. Human pancreatic carcinoma cells (PANC-1) in different groups and 24 mice with pancreatic cancer xenografts in four groups were treated with phosphate-buffered saline (PBS) as a control, RFH at 42 degrees C, gemcitabine and gemcitabine plus RFH at 42 degrees C. One day before and 1, 7 and 14 days after treatment, diffusion-weighted MRI and T2-weighted imaging were applied to monitor the apparent diffusion coefficients (ADCs) of tumors and tumor growth. MRI findings were correlated with the results of tumor apoptosis analysis. In the in vitro experiments, the quantitative viability assay showed lower relative cell viabilities for treatment with gemcitabine plus RFH at 42 degrees C relative to treatment with RFH only and gemcitabine only (37 +/- 5% versus 65 +/- 4% and 58 +/- 8%, respectively, p < 0.05). In the in vivo experiments, the combination therapy resulted in smaller relative tumor volumes than RFH only and chemotherapy only (0.82 +/- 0.17 versus 2.23 +/- 0.90 and 1.64 +/- 0.44, respectively, p = 0.003). In vivo, 14-T MRI demonstrated a remarkable decrease in ADCs at day 1 and increased ADCs at days 7 and 14 in the combination therapy group. The apoptosis index in the combination therapy group was significantly higher than those in the chemotherapy-only, RFH-only and PBS treatment groups (37 +/- 6% versus 20 +/- 5%, 8 +/- 2% and 3 +/- 1%, respectively, p < 0.05). This study confirms that it is feasible to use MRI to monitor RFH-enhanced chemotherapy in pancreatic cancers, which may present new options

for the efficient treatment of pancreatic malignancies using MRI/RFH-integrated local chemotherapy. Copyright © 2013 John Wiley & Sons, Ltd.

[111]

TÍTULO / TITLE: - Cisplatin-modified de gramont in second-line therapy for pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1138-42. doi: 10.1097/MPA.0b013e31829a80b7.

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

[1097/MPA.0b013e31829a80b7](#)

AUTORES / AUTHORS: - Ky V; Hav M; Berrevoet F; Troisi RI; Ferdinande L; Monsaert E; Vanderstraeten E; De Bosschere K; Van Damme N; Laurent S; Geboes K

INSTITUCIÓN / INSTITUTION: - From the *Department of Digestive Oncology, Ghent University Hospital, Ghent, Belgium; daggerCalmette Hospital, Phnom Penh, Cambodia; double daggerDepartment of Pathology, and section signDepartment of General and Hepatobiliary Surgery, Ghent University Hospital, Ghent, Belgium; parallelDepartment of Gastroenterology, Maria Middelaers Hospital, Ghent, Belgium; and paragraph signDepartment of Digestive Oncology, Ghent University Hospital, Ghent, Belgium.

RESUMEN / SUMMARY: - OBJECTIVES: In Belgium, combination chemotherapy of cisplatin and 5-fluorouracil + leucovorin (CFL) according to the modified de Gramont schedule is the treatment of choice in second line for metastatic pancreatic cancer. We retrospectively analyzed survival data in 2 Belgian centers in a nonselected population. METHODS: Between January 2004 and October 2011, 48 patients with histologically proven recurrent or unresectable pancreatic adenocarcinoma who had received CFL as second-line treatment were identified. We retrospectively analyzed the following parameters: progression-free survival (PFS1 and PFS2) for each line (after the start of first and second line), overall survival (OS), and growth modulation index. RESULTS: The median PFS1 was 5.4 months (95% confidence interval [CI], 4.1-6.6). The median PFS2 was 3.6 months (95% CI, 2-5.2). The median OS was 12 months (95% CI, 9.3-14.7). Twenty-three percent of patients had a growth modulation index >1.33. CONCLUSION: We show an OS of 12 months with gemcitabine in first-line and CFL in second-line therapy for pancreatic cancer. Sequential therapy with good OS and good quality of life may be preferred to strong upfront therapy in an incurable disease such as pancreatic cancer.

[112]

TÍTULO / TITLE: - Potential usefulness of mucin immunohistochemical staining of preoperative pancreatic biopsy or juice cytology specimens in the determination of treatment strategies for intraductal papillary mucinous neoplasm.

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

REVISTA / JOURNAL: - Oncol Rep. 2013 Nov;30(5):2035-41. doi: 10.3892/or.2013.2720. Epub 2013 Sep 5.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2720](#)

AUTORES / AUTHORS: - Hisaka T; Horiuchi H; Uchida S; Ishikawa H; Kawahara R; Kawashima Y; Akashi M; Mikagi K; Ishida Y; Okabe Y; Nakayama M; Naito Y; Yano H; Taira T; Kawahara A; Kage M; Kinoshita H; Shirozu K

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Kurume University School of Medicine, Kurume, Fukuoka 830-0011, Japan.

RESUMEN / SUMMARY: - We classified resected intraductal papillary mucinous neoplasms (IPMNs) into four subtypes (gastric, intestinal, pancreatobiliary and oncocytic) according to their morphological features and mucin expression, determined their clinicopathological characteristics and investigated the possibility of preoperatively diagnosing these subtypes. Sixty resected tumors, 4 preoperative tumor biopsies and 10 preoperative pancreatic juice cytology specimens were analyzed. The gastric and intestinal types accounted for the majority of IPMNs. Non-gastric type IPMNs were of high-grade malignancy. Many of the pancreatobiliary-type IPMNs were in an advanced stage and were associated with a poor prognosis. The results of mucin immunohistochemical staining of preoperative biopsy and surgically resected specimens were in agreement with each other, and in close agreement with those for pancreatic juice cytology specimens obtained from 10 patients during endoscopic retrograde cholangiopancreatography (ERCP). The immunostaining of preoperative biopsy specimens and ERCP-obtained pancreatic juice cytology specimens may be useful in the differential diagnosis of gastric and intestinal types of IPMN. If such techniques enable the preoperative diagnosis of IPMN subtypes, their use in combination with conventional preoperative imaging modalities may lead to surgical treatment best suited for the biological characteristics of the four subtypes.

[113]

TÍTULO / TITLE: - The association between the expression of solute carrier transporters and the prognosis of pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Sep;72(3):669-82. doi: 10.1007/s00280-013-2246-2. Epub 2013 Aug 11.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2246-2](#)

AUTORES / AUTHORS: - Mohelnikova-Duchonova B; Brynychova V; Hlavac V; Kocik M; Oliverius M; Hlavsa J; Honsova E; Mazanec J; Kala Z; Melichar B; Soucek P

INSTITUCIÓN / INSTITUTION: - Toxicogenomics Unit, National Institute of Public Health, Srobarova 48, 100 42, Prague 10, Czech Republic, D.Beatrice@seznam.cz.

RESUMEN / SUMMARY: - **OBJECTIVES:** The aim of this study was to investigate the prognostic significance of fourteen anticancer drug-relevant solute carrier transporters (SLCs) in pancreatic cancer in the context of clinical-pathological characteristics and the KRAS mutation status of tumors. **METHODS:** Tumors and non-neoplastic pancreatic tissues were obtained from 32 histologically verified patients with pancreatic ductal adenocarcinoma. The transcript profile of SLCs was assessed using quantitative real-time PCR. KRAS mutations in exon 2 were assessed by high-resolution melting analysis and confirmed by sequencing. **RESULTS:** SLC22A3 and SLC22A18 were upregulated and SLC22A1, SLC22A2, SLC22A11, SLC28A1, SLC28A3 and SLC29A1 were downregulated when compared with non-neoplastic pancreatic tissues. Moreover, significantly lower levels of SLC22A1, SLC22A11 and SLC29A1 were found in tumors with angioinvasion. There was also a significantly higher transcript level of SLC28A1 in tumors with regional lymph nodes affected by metastasis. The study found that a high expression of SLC28A1 was significantly associated with poor overall survival in unselected patients. In contrast, a high expression of SLC22A3 or SLC29A3 was significantly associated with longer overall survival in patients treated with nucleoside analogs. Protein expression of SLC22A1, SLC22A3 and SLC29A3 in tumor tissues of patients with pancreatic carcinoma was observed by immunoblotting for the first time. Finally, SLC levels were not found to be associated with KRAS mutation status in exon 2. **CONCLUSIONS:** This study identified a number of associations of transcript levels of SLCs with prognosis of pancreatic cancer patients.

[114]

TÍTULO / TITLE: - In vitro effects of lapatinib with gemcitabine for pancreatic cancer cells.

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

REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Aug;60(126):1484-7. doi: 10.5754/hge13195.

●● Enlace al texto completo (gratis o de pago) [5754/hge13195](#)

AUTORES / AUTHORS: - Murata A; Nakata B; Komoto M; Hirata K; Kimura K; Amano R; Hirakawa K

RESUMEN / SUMMARY: - **Background/Aims:** We investigated whether lapatinib plus gemcitabine has synergistic or antagonistic effects on the pancreatic cancer cell lines MiaPaca-2 and PANC-1. Furthermore, the changes of gemcitabine sensitivity-related genes by lapatinib treatment were examined. **Methodology:** The effects of lapatinib, gemcitabine, and combined treatment with both agents on cell viability were examined by methyl thiazolyl tetrazolium analysis. Synergy between lapatinib and gemcitabine was assessed by median effect analysis. The mRNA amounts of human equilibrative nucleoside transporter (hENT1), deoxycytidine kinase (dCK) and

ribonucleotide reductase subunit M1 (RRM1) genes were measured by quantitative real-time polymerase chain reaction in cells exposed to lapatinib for 48 h, as compared with untreated cells. Results: No synergistic effects were observed with combined treatment in either cell line. In contrast, antagonistic effects occurred on MiaPaca-2 cells with the two agents. Specific changes in gemcitabine sensitivity-related genes induced by lapatinib were not detected in either MiaPaca-2 or PANC-1. Conclusions: Lapatinib may not enhance the anti-tumor effects of gemcitabine for pancreatic cancer.

[115]

TÍTULO / TITLE: - Borderline Resectable/Locally Advanced Pancreatic Adenocarcinoma: Improvements Needed in Population-Based Registries.

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

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

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3237-6](#)

AUTORES / AUTHORS: - Miura JT; Evans DB; Pappas SG; Gamblin TC; Turaga KK

INSTITUCIÓN / INSTITUTION: - Division of Surgical Oncology, Medical College of Wisconsin, Milwaukee, WI, USA.

RESUMEN / SUMMARY: - BACKGROUND: Management of patients with borderline resectable/locally advanced (BR/LA) pancreatic adenocarcinoma is based on knowledge of natural history and patterns of treatment failure, information of great importance to large data registries. Using the SEER database, we examined the survival for patients with BR/LA tumors and critically evaluated the utility of the data. METHODS: T3/T4 tumors from 2004 to 2007 were divided into those that involved the portal vein/superior mesenteric vein/gastroduodenal artery/hepatic artery and those that involved the superior mesenteric artery (SMA) or celiac axis. The control group (CG) included patients who were recommended surgery but did not undergo it. Multivariate disease-specific survival analyses were performed using the Cox proportional hazards model. RESULTS: Of 3,837 patients, 571 patients (15 %) were recommended surgery, and 323 (8 %) underwent surgical resection. We were unable to separate patients into BR/LA based on current NCCN guidelines. We were able to identify vascular involvement but not those who actually underwent vascular resection. Median survival of patients who underwent surgery with SMA and celiac involvement was 12 and 8 months compared with 7 and 6 months, respectively, in the CG ($p = .01$). Patients who underwent surgical resection with venous involvement had a longer survival than those with arterial involvement (18 vs 12 months, $p = .001$). CONCLUSIONS: Analysis of patients with BR/LA pancreatic adenocarcinoma who underwent pancreatic resection in the SEER database yielded limited information. New manuals must focus on obtaining information consistent with current advances in the field; our recommendations for optimizing the SEER database are included.

[116]

TÍTULO / TITLE: - Minimally Invasive Ablation Treatment for Locally Advanced Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - Cardiovasc Intervent Radiol. 2013 Aug 30.

●● Enlace al texto completo (gratis o de pago) [1007/s00270-013-0724-x](#)

AUTORES / AUTHORS: - Rossi M; Orgera G; Hatzidakis A; Krokidis M

INSTITUCIÓN / INSTITUTION: - Unit of Interventional Radiology, S. Andrea University Hospital "Sapienza", Rome, Italy.

RESUMEN / SUMMARY: - Pancreatic adenocarcinoma is an aggressive tumour with an extremely poor prognosis, which has not changed significantly during the last 30 years. Prolonged survival is achieved only by R0 resection with macroscopic tumour clearance. However, the majority of the cases are considered inoperable at diagnosis due to local spread or presence of metastatic disease. Chemoradiotherapy is not tolerated by all patients and still fails to prolong survival significantly; neoadjuvant treatment also has limited results on pain control or tumour downstaging. In recent years, there has been a growing interest in the use of ablation therapy for the treatment of nonresectable tumours in various organs. Ablation techniques are based on direct application of chemical, thermal, or electrical energy to a tumour, which leads to cellular necrosis. With ablation, tumour cytoreduction, local control, and relief from symptoms are obtained in the majority of the patients. Inoperable cases of pancreatic adenocarcinoma have been treated by various ablation techniques in the last few years with promising results. The purpose of this review is to present the current status of local ablative therapies in the treatment of pancreatic adenocarcinoma and to investigate on the efficiency and the future trends.

[117]

TÍTULO / TITLE: - Large-cell neuroendocrine lung tumor presenting as acute pancreatitis.

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

REVISTA / JOURNAL: - Gastrointest Endosc. 2013 Aug 6. pii: S0016-5107(13)02085-3. doi: 10.1016/j.gie.2013.06.020.

●● Enlace al texto completo (gratis o de pago) [1016/j.gie.2013.06.020](#)

AUTORES / AUTHORS: - Dinis Silva J; Pinto Marques P; Brito MJ; Cortes J; Senhorinho R; Heredia V; Nunes A

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Hospital do Espírito Santo de Evora EPE, Evora, Portugal.

[118]

TÍTULO / TITLE: - Digalloylresveratrol, a novel resveratrol analog inhibits the growth of human pancreatic cancer cells.

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

REVISTA / JOURNAL: - Invest New Drugs. 2013 Oct;31(5):1115-24. doi: 10.1007/s10637-013-0009-x. Epub 2013 Aug 14.

●● Enlace al texto completo (gratis o de pago) [1007/s10637-013-0009-x](#)

AUTORES / AUTHORS: - Saiko P; Graser G; Giessrigl B; Steinmann MT; Schuster H; Lackner A; Grusch M; Krupitza G; Jaeger W; Somepalli V; Golakoti T; Fritzer-Szekeres M

INSTITUCIÓN / INSTITUTION: - Department of Medical and Chemical Laboratory Diagnostics, Medical University of Vienna, Waehringer Guertel 18-20, 1090, Vienna, Austria.

RESUMEN / SUMMARY: - Digalloylresveratrol (DIG) is a recently synthesized substance aimed to combine the effects of the natural polyphenolic compounds gallic acid and resveratrol, which both are excellent free radical scavengers with anticancer activity. In this study, we investigated the effects of DIG in the human AsPC-1 and BxPC-3 pancreatic adenocarcinoma cell lines. Treatment with DIG dose-dependently attenuated cells in the S phase of the cell cycle and led to a significant depletion of the dATP pool in AsPC-1 cells. The incorporation of (14)C-cytidine into nascent DNA of tumor cells was significantly inhibited at all DIG concentrations due to inhibition of ribonucleotide reductase, a key enzyme of DNA synthesis in tumor cells. Furthermore, Erk1/2 became inactivated and moderated p38 phosphorylation reflecting increased replication stress. DIG also activated ATM and Chk2, and induced the phosphorylation and proteasomal degradation of the proto-oncogene Cdc25A, which contributed to cell cycle attenuation. Taken together, DIG is an excellent free radical scavenger, strongly inhibits RR in situ activity, cell cycle progression, and colony formation in AsPC-1 and BxPC-3 cells thus warranting further investigations.

[119]

TÍTULO / TITLE: - Usefulness of pancreatic duct wire-guided endoscopic papillectomy for ampullary adenoma for preventing post-procedure pancreatitis.

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

REVISTA / JOURNAL: - Endoscopy. 2013 Oct;45(10):838-41. doi: 10.1055/s-0033-1344392. Epub 2013 Aug 5.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1344392](#)

AUTORES / AUTHORS: - Kim SH; Moon JH; Choi HJ; Kim DC; Lee TH; Cheon YK; Cho YD; Park SH; Kim SJ

INSTITUCIÓN / INSTITUTION: - Digestive Disease Center and Research Institute, Department of Internal Medicine, SoonChunHyang University School of Medicine, Bucheon and Seoul, Korea.

RESUMEN / SUMMARY: - Background and study aims: After endoscopic papillectomy, pancreatic duct stenting is important in preventing pancreatitis, but duct cannulation can be difficult following conventional snare resection. Pancreatic duct wire-guided endoscopic snaring before resection can reduce the post-procedure stenting failure rate. We evaluated the usefulness of this approach. Patients and methods: Pancreatic duct wire-guided endoscopic papillectomy was performed in 72 patients with ampullary adenoma. The snare loop was passed over a guide wire inserted into the pancreatic duct. After resection, a pancreatic stent was immediately placed along or alongside the guide wire. Results: Pancreatic duct stenting was successful in all patients after endoscopic papillectomy. Post-procedure pancreatitis occurred in 6/72 (8 %), but was mild and resolved with conservative treatment. Complete endoscopic resection of ampullary adenoma was achieved in 65/72 (90 %), with en bloc resection in 60/72 (83 %). There was no procedure-associated mortality. Follow-up (mean 23.7 months) showed recurrence in 5/65 (8 %) who had undergone complete resection. Conclusions: Pancreatic duct wire-guided endoscopic snare papillectomy for ampullary adenoma effectively facilitated pancreatic duct stenting to prevent severe post-procedure pancreatitis.

[120]

TÍTULO / TITLE: - Prognostic significance of extracellular matrix degrading enzymes-cathepsin L and matrix metalloproteases-2 [MMP-2] in human pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Invest. 2013 Aug;31(7):461-71. doi: 10.3109/07357907.2013.820318.

●● Enlace al texto completo (gratis o de pago) [3109/07357907.2013.820318](https://doi.org/10.3109/07357907.2013.820318)

AUTORES / AUTHORS: - Singh N; Das P; Datta Gupta S; Sahni P; Pandey RM; Gupta S; Chauhan SS; Saraya A

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology & Human Nutrition, All India Institute of Medical Sciences, New Delhi, India.

RESUMEN / SUMMARY: - In the present study, we assessed the expression of extracellular matrix (ECM) degrading proteases-cathepsin L and matrix metalloprotease-2 (MMP-2) in pancreatic cancer tissue and correlated their levels with clinicopathological parameters and survival. Both the proteases were expressed in the majority of the tumor tissues examined. Staining intensity of cathepsin L was significantly higher in the tumor stroma compared to tumor epithelium while MMP-2 staining showed no such difference. Both proteases showed correlation with some of the clinicopathological parameters but only cathepsin L expression in tumor epithelium predicted a poor prognosis for the disease.

[121]

TÍTULO / TITLE: - Indometacin ameliorates high glucose-induced proliferation and invasion via modulation of e-cadherin in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Curr Med Chem. 2013;20(33):4142-52.

AUTORES / AUTHORS: - Han L; Peng B; Ma Q; Ma J; Li J; Li W; Duan W; Chen C; Liu J; Xu Q; Laporte K; Li Z; Wu E

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, The First Affiliated Hospital of Medical College, Xi' an Jiaotong University, 277 West Yanta Road, Xi' an 710061, Shaanxi, China. gyms56@mail.xjtu.edu.cn.

RESUMEN / SUMMARY: - Indometacin, an inhibitor of cyclooxygenase-2 (COX-2), has been shown to exert anticancer effects in a variety of cancers. However, the effect and mechanism of indometacin on high glucose (HG)-induced proliferation and invasion of pancreatic cancer (PC) cells remain unclear. Multiple lines of evidence suggest that a large portion of pancreatic cancer (PC) patients suffer from either diabetes or HG which contributing PC progression. In this study, we report that indometacin down-regulated HG-induced proliferation and invasion via up-regulating E-cadherin but not COX-2 in PC cells. Additionally, the E-cadherin transcriptional repressors, Snail and Slug, were also involved in the process. Furthermore, the proliferation and invasion of PC cells, incubated in HG medium and treated with indometacin were significantly increased when E-cadherin was knocked down (Si-E-cad). Moreover, the protein levels of MMP-2, MMP-9, and VEGF were increased in PC cells transfected with Si-E-cad. Finally, the activation of the PI3K/AKT/GSK-3beta signaling pathway was demonstrated to be involved in indometacin reversing HG-induced cell proliferation and invasion in PC cells. In conclusion, these results suggest that indometacin plays a key role in down-regulating HG-induced proliferation and invasion in PC cells. Our findings indicate that indometacin could be used as a novel therapeutic strategy to treat PC patients who simultaneously suffer from diabetes or HG.

[122]

TÍTULO / TITLE: - Impact of Tumor Grade on Pancreatic Cancer Prognosis: Validation of a Novel TNMG Staging System.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Aug 14.

●● [Enlace al texto completo \(gratis o de pago\) 1245/s10434-013-3159-3](#)

AUTORES / AUTHORS: - Rochefort MM; Ankeny JS; Kadera BE; Donald GW; Isacoff W; Wainberg ZA; Hines OJ; Donahue TR; Reber HA; Tomlinson JS

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Greater Los Angeles VA Healthcare System, Los Angeles, CA, USA.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic ductal adenocarcinoma (PDAC) patients demonstrate highly variable survival within each stage of the American Joint Committee on Cancer (AJCC) staging system. We hypothesize that tumor grade is partly responsible for this variation. Recently our group developed a novel tumor, node, metastasis, grade (TNMG) classification system utilizing Surveillance Epidemiology and End Results (SEER) data in which the presence of high tumor grade results in advancement to the next higher AJCC stage. This study's objective was to validate this TNMG staging system utilizing single-institution data. METHODS: All patients with PDAC who underwent resection at UCLA between 1990 and 2009 were identified. Clinicopathologic data reviewed included age, sex, node status, tumor size, grade, and stage. Grade was redefined as a dichotomous variable. The impact of grade on survival was assessed by Cox regression analysis. Disease was restaged into the TNMG system and compared to the AJCC staging system. RESULTS: We identified 256 patients who underwent resection for PDAC. Patients with low-grade tumors experienced a 13-month improvement in median survival compared to those with high-grade tumors. On multivariate analysis, tumor grade was the strongest predictor of survival with a hazard ratio of 2.02 (p = 0.0005). Restaging disease according to the novel TNMG staging system resulted in improved survival discrimination between stages compared to the current AJCC system. CONCLUSIONS: We were able to demonstrate that grade is one of the strongest independent prognostic factors in PDAC. Restaging with our novel TNMG system demonstrated improved prognostication. This system offers an effective and convenient way of adding grade to the current AJCC staging system.

[123]

TÍTULO / TITLE: - The value of mutational profiling of the cytocentrifugation supernatant fluid from fine-needle aspiration of pancreatic solid mass lesions.

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

REVISTA / JOURNAL: - Mod Pathol. 2013 Sep 20. doi: 10.1038/modpathol.2013.147.

●● Enlace al texto completo (gratis o de pago) [1038/modpathol.2013.147](#)

AUTORES / AUTHORS: - Deftereos G; Finkelstein SD; Jackson SA; Ellsworth EM; Krishnamurti U; Liu Y; Silverman JF; Binkert CR; Ujevich BA; Mohanty A

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Laboratory Medicine, Allegheny General Hospital, Pittsburgh, PA, USA.

RESUMEN / SUMMARY: - Fine-needle aspiration (FNA) of pancreatic solid masses can be significantly impacted by sampling variation. Molecular analysis of tumor DNA can be an aid for more definitive diagnosis. The aim of this study was to evaluate how molecular analysis of the cell-free cytocentrifugation supernatant DNA can help reduce sampling variability and increase diagnostic yield. Twenty-three FNA smears from pancreatic solid masses were performed. Remaining aspirates were rinsed for

preparation of cytocentrifuged slides or cell blocks. DNA was extracted from supernatant fluid and assessed for DNA quantity spectrophotometrically and for amplifiability by quantitative PCR (qPCR). Supernatants with adequate DNA were analyzed for mutations using PCR/capillary electrophoresis for a broad panel of markers (KRAS point mutation by sequencing, microsatellite fragment analysis for loss of heterozygosity (LOH) of 16 markers at 1p, 3p, 5q, 9p, 10q, 17p, 17q, 21q, and 22q). In selected cases, microdissection of stained cytology smears and/or cytocentrifugation cellular slides were analyzed and compared. In all, 5/23 samples cytologically confirmed as adenocarcinoma showed detectable mutations both in the microdissected slide-based cytology cells and in the cytocentrifugation supernatant. While most mutations detected were present in both microdissected slides and supernatant fluid specimens, the latter showed additional mutations supporting greater sensitivity for detecting relevant DNA damage. Clonality for individual marker mutations was higher in the supernatant fluid than in microdissected cells. Cytocentrifugation supernatant fluid contains levels of amplifiable DNA suitable for mutation detection and characterization. The finding of additional detectable mutations at higher clonality indicates that supernatant fluid may be enriched with tumor DNA. Molecular analysis of the supernatant fluid could serve as an adjunct method to reduce sampling variability and increase diagnostic yield, especially in cases with a high clinical suspicion for malignancy and limited number of atypical cells in the smears. Modern Pathology advance online publication, 20 September 2013; doi:10.1038/modpathol.2013.147.

[124]

TÍTULO / TITLE: - Resveratrol Inhibits the Epithelial-Mesenchymal Transition of Pancreatic Cancer Cells Via Suppression of the PI-3K/Akt/NF-kappaB Pathway.

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

REVISTA / JOURNAL: - Curr Med Chem. 2013;20(33):4185-94.

AUTORES / AUTHORS: - Li W; Ma J; Ma Q; Li B; Han L; Liu J; Xu Q; Duan W; Yu S; Wang F; Wu E

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, The First Affiliated Hospital of Medical College, Xi'an Jiaotong University, 277 West Yanta Road, Xi'an 710061, Shaanxi, China. gyms56@mail.xjtu.edu.cn.

RESUMEN / SUMMARY: - Resveratrol (trans-3,4',5-trihydroxystilbene), a natural polyphenolic compound detected in grapes, berries, and peanuts, possesses a wide spectrum of pharmacological properties, including anti-tumor metastasis activities. However, the underlying mechanisms through which resveratrol inhibits the metastasis of pancreatic cancer are still not fully elucidated. As epithelial-to-mesenchymal transition (EMT) is a key player for metastasis in tumor, the aim of this study is to determine whether resveratrol affects EMT in pancreatic cancer cells and

the related mechanism. The results showed that resveratrol not only inhibited cell proliferation, migration, and invasion in a dose-dependent manner, but also mediated the expression of EMT-related genes (E-cadherin, N-cadherin, vimentin, MMP-2, and MMP-9) which are important for cancer cellular motility, invasiveness and metastasis during tumorigenesis. In addition, the levels of phospho-Akt and phospho- NF-kappaB in BxPC-3 and Panc-1 cells were reduced by both resveratrol and LY294002 (a PI3-K inhibitor). Furthermore, transforming growth factor-beta (TGF-beta)-induced alterations in cell morphology that are characteristic of EMT as well as increased cell invasive ability could also be reversed by resveratrol. Taken together, these data indicate that resveratrol suppresses pancreatic cancer migration and invasion through the inhibition of the PI-3K/Akt/NF-kappaB signaling pathway. This study suggests that resveratrol may be a potential anticancer agent for pancreatic cancer.

[125]

TÍTULO / TITLE: - A novel epidermal growth factor receptor-signaling platform and its targeted translation in pancreatic cancer.

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

REVISTA / JOURNAL: - Cell Signal. 2013 Aug 30;25(12):2587-2603. doi: 10.1016/j.cellsig.2013.08.008.

●● Enlace al texto completo (gratis o de pago) [1016/j.cellsig.2013.08.008](#)

AUTORES / AUTHORS: - Gilmour AM; Abdulkhalek S; Cheng TS; Alghamdi F; Jayanth P; O'Shea LK; Geen O; Arvizu LA; Szewczuk MR

INSTITUCIÓN / INSTITUTION: - Department of Biomedical & Molecular Sciences, Queen's University, Kingston, ON K7L3N6, Canada. Electronic address:

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RESUMEN / SUMMARY: - Epidermal growth factor (EGF)-induced EGFR tyrosine kinase receptor activation in cancer cell survival responses has become a strategic molecular-targeting clinical therapeutic intent, but the failures of these targeted approaches in the clinical setting demand alternate strategies. Here, we uncover a novel neuraminidase-1 (Neu1) and matrix metalloproteinase-9 (MMP-9) cross-talk in alliance with GPCR neuromedin B, which is essential for EGF-induced receptor activation and cellular signaling. Neu1 and MMP-9 form a complex with EGFR on the cell surface. Tamiflu (oseltamivir phosphate), anti-Neu1 antibodies, broad range MMP inhibitor galardin (GM6001), neuromedin B GPCR specific antagonist BIM-23127, the selective inhibitor of whole heterotrimeric G-protein complex BIM-46174 and MMP-9 specific inhibitor dose-dependently inhibited Neu1 activity associated with EGF stimulated 3T3-hEGFR cells. Tamiflu, anti-Neu1 antibodies and MMP9i attenuated EGFR phosphorylation associated with EGF-stimulated cells. Preclinical data provide the proof-of-evidence for a therapeutic targeting of Neu1 with Tamiflu in impeding human pancreatic cancer growth and metastatic spread in heterotopic xenografts of eGFP-

MiaPaCa-2 tumors growing in RAGxCgamma double mutant mice. Tamiflu-treated cohort exhibited a reduction of phosphorylation of EGFR-Tyr1173, Stat1-Tyr701, Akt-Thr308, PDGFRalpha-Tyr754 and NfKappaBp65-Ser311 but an increase in phospho-Smad2-Ser465/467 and -VEGFR2-Tyr1175 in the tumor lysates from the xenografts of human eGFP-MiaPaCa-2 tumor-bearing mice. The findings identify a novel promising alternate therapeutic treatment of human pancreatic cancer.

[126]

TÍTULO / TITLE: - Pancreatic Cancer.

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

REVISTA / JOURNAL: - Br J Pharmacol. 2013 Sep 11. doi: 10.1111/bph.12401.

●● [Enlace al texto completo \(gratis o de pago\) 1111/bph.12401](#)

AUTORES / AUTHORS: - Gungor C; Hofmann BT; Wolters-Eisfeld G; Bockhorn M

INSTITUCIÓN / INSTITUTION: - Department of General-, Visceral- and Thoracic Surgery, Experimental Oncology, Campus Research, University Hospital Hamburg-Eppendorf, Martinistrasse 52, 20246, Hamburg, Germany.

RESUMEN / SUMMARY: - In recent years, it becomes evident that current standard therapeutic options for pancreatic cancer are not sufficient enough and still do not meet the criteria to cure more efficiently patients that suffer from this deadly disease. Although the research of the latest decade showed very interesting and promising new therapeutic options for these patients, only minor success was clinically displayed, unfortunately. Therefore, pancreatic cancer is highly linked with the urgent necessity of new approaches that deal with early detection and new therapy options. In fact, to provide optimal care for pancreatic cancer patients, continuous investigations are crucial and will help to better understand its complex molecular biology, which in turn, is accompanied by the identification of new target molecules that may promote the progression and therapy resistance of pancreatic cancer cells. Despite significant effort directed at curing cancers with chemotherapy, pancreatic cancer is one of the most resistant cancer among solid tumors and many studies suggest that drug-resistant cancer cells are the most aggressive ones with highest relapse and metastatic rates. In line with this, it was recently shown that activated notch signaling is strongly linked with chemoresistance and therefore reflects a rationale new target to circumvent chemotherapy-resistance in pancreatic cancer. In summary, we focus our discussion in this review on latest research breakthroughs, current therapy options and recently identified target molecules such as Notch-2 and the heparin-binding growth-factor Midkine, that promote a plethora of cancer-relevant features and implicates therefore attractive new therapeutical target molecules in other cancers as well.

[127]

TÍTULO / TITLE: - Role of second-line chemotherapy in advanced pancreatic cancer and its influence on phase II/III study results.

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

REVISTA / JOURNAL: - Ann Oncol. 2013 Sep;24(9):2462-3. doi: 10.1093/annonc/mdt296.

●● Enlace al texto completo (gratis o de pago) [1093/annonc/mdt296](#)

AUTORES / AUTHORS: - Teo M; McDermott RS

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Adelaide & Meath Hospital, incorporating National Children's Hospital, Tallaght, Dublin 24, Ireland.

[128]

TÍTULO / TITLE: - Metformin and survival in pancreatic cancer: a retrospective cohort study.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1054-9. doi:

10.1097/MPA.0b013e3182965a3c.

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

[1097/MPA.0b013e3182965a3c](#)

AUTORES / AUTHORS: - Hwang AL; Haynes K; Hwang WT; Yang YX

INSTITUCIÓN / INSTITUTION: - From the *Division of Gastroenterology, Hospital at the University of Pennsylvania; and daggerCenter for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, PA.

RESUMEN / SUMMARY: - **OBJECTIVES:** Our aim was to determine the effect of metformin exposure on survival in patients with advanced pancreatic adenocarcinoma (PAC). **METHODS:** A retrospective cohort study was conducted using The Health Improvement Network, a primary care electronic medical record database from the United Kingdom (2003-2010). The study cohort included all subjects with a diagnostic code for incident PAC and a preexisting diagnosis of type 2 diabetes mellitus. Subjects were classified as exposed if they were prescribed metformin around the time of PAC diagnosis (between 6 months prior and 1 month after). A secondary analysis was performed only on exposed subjects without prior (ie, 6 months before PAC diagnosis) exposure to metformin. The primary outcome was overall survival. The analysis was performed using univariate and multivariable Cox proportional hazards models. **RESULTS:** The study included 516 subjects with preexisting type 2 diabetes mellitus and PAC, 247 of which were exposed to metformin. In univariate and multivariable analysis, there was no difference in survival between those exposed and those unexposed to metformin in the primary analysis (hazards ratio, 1.11 [0.89-1.38], P = 0.367) or the secondary analysis (hazards ratio, 1.09 [0.80-1.47], P = 0.585). **CONCLUSIONS:** Metformin use is not associated with improved survival in subjects with advanced PAC.

[129]

TÍTULO / TITLE: - Novel synthetic curcumin analogues EF31 and UBS109 are potent DNA hypomethylating agents in pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Lett. 2013 Aug 7. pii: S0304-3835(13)00575-2. doi: 10.1016/j.canlet.2013.08.002.

●● Enlace al texto completo (gratis o de pago) [1016/j.canlet.2013.08.002](#)

AUTORES / AUTHORS: - Nagaraju GP; Zhu S; Wen J; Farris AB; Adsay VN; Diaz R; Snyder JP; Mamoru S; El-Rayes BF

INSTITUCIÓN / INSTITUTION: - Department of Hematology and Medical Oncology, Emory University, Atlanta, GA, United States.

RESUMEN / SUMMARY: - DNA methylation is a rational therapeutic target in pancreatic cancer. The activity of novel curcumin analogues EF31 and UBS109 as demethylating agents were investigated. MiaPaCa-2 and PANC-1 cells were treated with vehicle, curcumin, EF31 or UBS109. EF31 and UBS109 resulted in significantly higher inhibition of proliferation and cytosine methylation than curcumin. Demethylation was associated with re-expression of silenced p16, SPARC, and E-cadherin. EF31 and UBS109 inhibited HSP-90 and NF-kappaB leading to downregulation of DNA methyltransferase-1 (DNMT-1) expression. Transfection experiments confirmed this mechanism of action. Similar results were observed in vitro when subcutaneous tumors (MiaPaCa-2) were treated with EF31 and UBS109.

[130]

TÍTULO / TITLE: - Stromal disrupting effects of nab-paclitaxel in pancreatic cancer.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Aug 20;109(4):926-33. doi: 10.1038/bjc.2013.415. Epub 2013 Aug 1.

●● Enlace al texto completo (gratis o de pago) [1038/bjc.2013.415](#)

AUTORES / AUTHORS: - Alvarez R; Musteanu M; Garcia-Garcia E; Lopez-Casas PP; Megias D; Guerra C; Munoz M; Quijano Y; Cubillo A; Rodriguez-Pascual J; Plaza C; de Vicente E; Prados S; Taberero S; Barbacid M; Lopez-Rios F; Hidalgo M

INSTITUCIÓN / INSTITUTION: - Centro Integral Oncologico Clara Campal (CIOCC), Ona 10, 28050 Madrid, España.

RESUMEN / SUMMARY: - Background:Nab-paclitaxel and gemcitabine have demonstrated a survival benefit over gemcitabine alone in advanced pancreatic cancer (PDA). This study aimed to investigate the clinical, biological, and imaging effects of the regimen in patients with operable PDA.Methods:Patients with operable PDA received two cycles of nab-paclitaxel and gemcitabine before surgical resection. FDG-PET and CA19.9 tumour marker levels were used to measure clinical activity. Effects on tumour stroma were determined by endoscopic ultrasound (EUS) elastography. The collagen content

and architecture as well as density of cancer-associated fibroblasts (CAFs) were determined in the resected surgical specimen and compared with a group of untreated and treated with conventional chemoradiation therapy controls. A co-clinical study in a mouse model of PDA was conducted to differentiate between the effects of nab-paclitaxel and gemcitabine. Results: A total of 16 patients were enrolled. Treatment resulted in significant antitumour effects with 50% of patients achieving a >75% decrease in circulating CA19.9 tumour marker and a response by FDG-PET. There was also a significant decrement in tumour stiffness as measured by EUS elastography. Seven of 12 patients who completed treatment and were operated had major pathological regressions. Analysis of residual tumours showed a marked disorganised collagen with a very low density of CAF, which was not observed in the untreated or conventionally treated control groups. The preclinical co-clinical study showed that these effects were specific of nab-paclitaxel and not gemcitabine. Conclusion: These data suggest that nab-paclitaxel and gemcitabine decreases CAF content inducing a marked alteration in cancer stroma that results in tumour softening. This regimen should be studied in patients with operable PDA.

[131]

TÍTULO / TITLE: - Target Therapies In Pancreatic Carcinoma.

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

REVISTA / JOURNAL: - Curr Med Chem. 2013 Aug 23.

AUTORES / AUTHORS: - Silvestris N; Gnoni A; Brunetti AE; Vincenti L; Santini D; Tonini G; Merchionne F; Maiello E; Lorusso V; Nardulli P; Azzariti A; Reni M

INSTITUCIÓN / INSTITUTION: - Medical Oncology Unit, National Cancer Research Centre - Istituto Tumori Giovanni Paolo II, Viale Orazio Flacco, 65, 70124 Bari, Italy.

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RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) occurs in the majority of cases with early locoregional spread and distant metastases at diagnosis, leading to dismal prognosis and limited treatment options. Traditional cytotoxic chemotherapy provides only modest benefit to patients with PDAC. Identification of different molecular pathways, overexpressed in pancreatic cancer cells, has provided the opportunity to develop targeted therapies (monoclonal antibodies and small-molecule inhibitors) and peculiar new class of taxanes with a crucial therapeutic role in this cancer setting. A phase III trial has shown that erlotinib in combination with gemcitabine was clinically irrelevant and skin toxicity can be a positive prognostic factor. Moreover, the combination of cetuximab or erlotinib with radiotherapy in advanced pancreatic cancer has shown to be synergistic and a reversal of radio-resistance has been suggested by inhibition of VEGF/EGFR pathway. To overcome EGFR-inhibition therapy resistance several alternative pathways targets are under

investigation (IGF-1R, MMPs, Hedgehog proteins, m-TOR, MEK, COX-2) and provide the rationale for clinical use in phase II/III studies. Also nab-paclitaxel, a new taxanes class, uses high pancreatic albumin-binding protein SPARC levels to act in cancer cells with a less toxic and more effective dose with respect to classic taxanes. Understanding of molecular pathogenesis of pancreatic adenocarcinoma continues to expand. However, many promising data in preclinic and phase I/II trials did not yield promise in phase III trials, suggesting that identification of predictive biomarkers for these new agents is mandatory. The knowledge of biologic and molecular aspects of pancreatic cancer can be the basis for future therapeutic developments.

[132]

TÍTULO / TITLE: - Metastatic Pancreatic Adenocarcinoma to the Mandibular Condyle: A Rare Clinical Presentation.

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

REVISTA / JOURNAL: - J Oral Maxillofac Surg. 2013 Aug 1. pii: S0278-2391(13)00812-4. doi: 10.1016/j.joms.2013.06.207.

●● Enlace al texto completo (gratis o de pago) 1016/j.joms.2013.06.207

AUTORES / AUTHORS: - Kolokythas A; Miloro MB; Olsson AB; Miloro M

INSTITUCIÓN / INSTITUTION: - Assistant Professor, Department of Oral and Maxillofacial Surgery, and Member, Cancer Center, University of Illinois at Chicago, Chicago, IL. Electronic address: mmiloro@uic.edu.

RESUMEN / SUMMARY: - Metastatic disease to the oral cavity is rare, representing only 1-8% of oral malignancies, and involvement of the mandibular condyle is even less prevalent. In a recent literature review of 796 cases of metastatic disease to the oral cavity, only 39 (13.8%) involved the condyle. This report is a unique case of metastatic pancreatic adenocarcinoma to the condyle. There are only 5 documented cases of metastatic pancreatic adenocarcinoma to the oral cavity, one of which metastasized to the condyle. This is an important case because metastatic lesions to the condyle may mimic temporomandibular joint disorders making clinical diagnosis and decision-making extremely challenging for the oral and maxillofacial surgeon. The requirement for arrival at an appropriate and prompt diagnosis is crucial for determining the most appropriate treatment regimens and improved outcomes. Additionally, in approximately 33% of cases, the oral metastatic lesion may be the first indication of an undiscovered distant primary tumor, making timely evaluation and treatment critical from an oncologic perspective.

[133]

TÍTULO / TITLE: - Quantitative magnetization transfer MRI of desmoplasia in pancreatic ductal adenocarcinoma xenografts.

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

REVISTA / JOURNAL: - NMR Biomed. 2013 Aug 12. doi: 10.1002/nbm.3004.

●● Enlace al texto completo (gratis o de pago) [1002/nbm.3004](#)

AUTORES / AUTHORS: - Li W; Zhang Z; Nicolai J; Yang GY; Omary RA; Larson AC

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA.

RESUMEN / SUMMARY: - Quantitative assessment of desmoplasia in pancreatic ductal adenocarcinoma (PDAC) may be critical for staging or prediction of response to therapy. We performed quantitative magnetization transfer (qMT) MRI measurements in 18 mouse xenograft tumors generated from three PDAC cell lines. The qMT parameter bound proton fraction (BPF) was found to be significantly higher in tumors grown using the BxPC-3 cell line (5.31 +/- 0.87, mean +/- standard deviation) compared with the BPF measured for tumors grown from Panc-1 (3.65 +/- 0.60) and Capan-1 (1.50 +/- 0.58) cell lines (P < 0.05 for each comparison). Histologic measurements demonstrated a similar trend; BxPC-3 tumors had significantly higher fibrosis levels (percentage of fibrotic tissue area, 6.21 +/- 2.10) compared with Panc-1 (2.88 +/- 1.13) and Capan-1 (1.69 +/- 1.01) tumors. BPF was well correlated with quantitative fibrosis levels (r = 0.77, P < 0.01). Our results indicate that qMT measurements offer the potential to noninvasively quantify fibrosis levels in PDAC mouse xenograft models and thus serve as a valuable in vivo biomarker of desmoplasia in PDAC. Copyright © 2013 John Wiley & Sons, Ltd.

[134]

TÍTULO / TITLE: - Is diabetes mellitus a risk factor for pancreatic cancer?

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Aug 14;19(30):4861-6. doi: 10.3748/wjg.v19.i30.4861.

●● Enlace al texto completo (gratis o de pago) [3748/wjg.v19.i30.4861](#)

AUTORES / AUTHORS: - Pezzilli R; Pagano N

INSTITUCIÓN / INSTITUTION: - Raffaele Pezzilli, Nico Pagano, Department of Digestive Diseases and Internal Medicine, Sant'Orsola-Malpighi Hospital, 40138 Bologna, Italy.

RESUMEN / SUMMARY: - The relationship between diabetes mellitus and the risk of pancreatic cancer has been a matter of study for a long period of time. The importance of this topic is due to two main causes: the possible use of recent onset diabetes as a marker of the disease and, in particular, as a specific marker of pancreatic cancer, and the selection of a population at risk for pancreatic cancer. Thus, we decided to make an in-depth study of this topic; thus, we carried out an extensive literature search in order to re-assess the current knowledge on this topic. Even if diabetes is found a decade before the appearance of pancreatic cancer as reported in meta-analytic studies, we cannot select those patients already having non detectable

pancreatic cancer, at least with the imaging and biological techniques available today. We believe that more studies are necessary in order to definitively identify diabetes mellitus as a risk factor for pancreatic cancer taking into consideration that approximately 10 years are needed to diagnose symptomatic pancreatic cancer. At present, the answer to the as to whether diabetes and pancreatic cancer comes first similar to the adage of the chicken and the egg is that diabetes is the egg.

[135]

TÍTULO / TITLE: - Margin status, recurrence pattern, and prognosis after resection of pancreatic cancer.

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

REVISTA / JOURNAL: - Surgery. 2013 Aug 22. pii: S0039-6060(13)00162-1. doi: 10.1016/j.surg.2013.04.015.

●● Enlace al texto completo (gratis o de pago) [1016/j.surg.2013.04.015](#)

AUTORES / AUTHORS: - Sugiura T; Uesaka K; Mihara K; Sasaki K; Kanemoto H; Mizuno T; Okamura Y

INSTITUCIÓN / INSTITUTION: - Division of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center, Shizuoka, Japan. Electronic address: t.sugiura@scchr.jp.

RESUMEN / SUMMARY: - BACKGROUND: Controversy persists as to whether positive operative margins are an independent prognostic factor for resected pancreatic cancer. This study evaluated the impact of the resection margin status on the patterns of recurrence and prognosis after resection for pancreatic cancer. METHODS: A total of 208 patients with pancreatic cancer who underwent resection with curative intent were studied retrospectively. All patients underwent pancreatectomy (164 pancreatoduodenectomies, 42 distal pancreatectomies, and 2 total pancreatectomies) intended to achieve R0 resection. They were divided into three groups on the basis of the following margin status: R>1 mm, R0-1 mm, and R0 mm. The postoperative survival and recurrence patterns were evaluated in relation to the margin status. Multivariate analyses were performed to evaluate the factors influencing the overall survival. RESULTS: The resection margin was R>1 mm in 134 patients (65%), R0-1 mm in 40 (19%), and R0 mm in 34 patients (16%). The margin status correlated with the rate of local recurrence; 8% in R>1 mm, 20% in R0-1 mm, and 50% in R0 mm patients. In contrast, the incidence of recurrence at other sites, such as the lymph nodes, peritoneum, liver and other distant organs, were almost identical among the three groups. The median survival time was 26 months in R>1 mm, 30 months in R0-1 mm, and 23 months in R0 mm patients (P = not significant). The multivariate analyses revealed that lymph node metastases and poor differentiation were correlated with poor survival. CONCLUSION: In the setting of pancreatectomy, when we evaluated the definitions of R0 resection, the margin status influenced the local recurrence rate but had no impact on the patients' survival.

[136]

TÍTULO / TITLE: - Cracking the stone: combination vaccination and CTLA-4 blockade in pancreatic cancer.

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

REVISTA / JOURNAL: - J Immunother. 2013 Sep;36(7):362-4. doi: 10.1097/CJI.0b013e31829fb7c8.

●● Enlace al texto completo (gratis o de pago) [1097/CJI.0b013e31829fb7c8](#)

AUTORES / AUTHORS: - Bajor DL; Vonderheide RH

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Abramson Family Cancer Research Institute, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA.

[137]

TÍTULO / TITLE: - Role of hypoxia inducible factor-1alpha in the regulation of the cancer-specific variant of organic anion transporting polypeptide 1B3 (OATP1B3), in colon and pancreatic cancer.

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

REVISTA / JOURNAL: - Biochem Pharmacol. 2013 Sep 15;86(6):816-23. doi: 10.1016/j.bcp.2013.07.020. Epub 2013 Aug 4.

●● Enlace al texto completo (gratis o de pago) [1016/j.bcp.2013.07.020](#)

AUTORES / AUTHORS: - Han S; Kim K; Thakkar N; Kim D; Lee W

INSTITUCIÓN / INSTITUTION: - Department of Biological Sciences, Konkuk University, Seoul 143-701, Republic of Korea.

RESUMEN / SUMMARY: - Organic anion transporting polypeptide 1B3 (OATP1B3) was initially considered to be a liver-specific transporter, mediating the uptake of a variety of endogenous and xenobiotic substances. Over the past decade, several investigations reported that OATP1B3 is also expressed across multiple types of cancers. Only recently, our laboratory and others demonstrated the identity of cancer-specific OATP1B3 variants (csOATP1B3) arising from the use of an alternative transcription initiation site, different from the wildtype (WT) OATP1B3 expressed in the normal liver. However, the mechanisms regulating the expression of csOATP1B3 remained unknown. In our current study, we investigated the role of hypoxia and the involvement of hypoxia inducible factor-1alpha (HIF-1alpha) in regulating the transcription of csOATP1B3. Our RT-PCR and immunoblotting results indicated that csOATP1B3, but not WT OATP1B3, can be induced in response to ambient or chemical hypoxia (upon exposure to 1% O₂ or cobalt chloride). Reporter assays with deletion and mutated constructs of the csOATP1B3 promoter revealed a functional hypoxia response element (HRE) located in the proximal upstream region. Constructs harboring

the HRE displayed the upregulated reporter gene expression in response to hypoxia, but not when mutated. Electrophoretic mobility shift assays using a biotin-labeled csOATP1B3 promoter HRE probe indicated the binding of HIF-1alpha, which was blocked by an excess of unlabeled csOATP1B3 probe. Furthermore, siRNA-based knockdown of HIF-1alpha caused a substantial decrease in the expression level of csOATP1B3. Taken together, these findings demonstrate that the transcription of csOATP1B3 is actively engaged during hypoxia, through a commonly utilized pathway involving HIF-1alpha.

[138]

TÍTULO / TITLE: - A binuclear complex constituted by diethyldithiocarbamate and copper(I) functions as a proteasome activity inhibitor in pancreatic cancer cultures and xenografts.

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

REVISTA / JOURNAL: - Toxicol Appl Pharmacol. 2013 Sep 20. pii: S0041-008X(13)00409-2. doi: 10.1016/j.taap.2013.09.009.

●● Enlace al texto completo (gratis o de pago) [1016/j.taap.2013.09.009](#)

AUTORES / AUTHORS: - Han J; Liu L; Yue X; Chang J; Hua Y

INSTITUCIÓN / INSTITUTION: - Department of Integrative Oncology, Fudan University Shanghai Cancer Center, Shanghai 200032, China; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, China; Shanghai Clinical Center, Chinese Academy of Sciences/Xuhui Central Hospital, Shanghai 200031, China. Electronic address: hanjinbin@gmail.com.

RESUMEN / SUMMARY: - It is a therapeutic strategy for cancers including pancreatic to inhibit proteasome activity. Disulfiram (DSF) may bind copper (Cu) to form a DSF-Cu complex. DSF-Cu is capable of inducing apoptosis in cancer cells by inhibiting proteasome activity. DSF is rapidly converted to diethyldithiocarbamate (DDTC) within bodies. Copper(II) absorbed by bodies is reduced to copper(I) when it enters cells. We found that DDTC and copper(I) could form a binuclear complex which might be entitled DDTC-Cu(I), and it had been synthesized by us in the laboratory. This study is to investigate the anticancer potential of this complex on pancreatic cancer and the possible mechanism. Pancreatic cancer cell lines, SW1990, PANC-1 and BXPC-3 were used for in vitro assays. Female athymic nude mice grown SW1990 xenografts were used as animal models. Cell counting kit-8 (cck-8) assay and flow cytometry were used for analyzing apoptosis in cells. A 20S proteasome assay kit was used in proteasome activity analysis. Western blot (WB) and immunohistochemistry (IHC) and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assays were used in tumor sample analysis. The results suggest that DDTC-Cu(I) inhibit pancreatic cancer cell proliferation and proteasome activity in vitro and in vivo. Accumulation of ubiquitinated proteins, and increased p27 as well as decreased NF-kappaB expression

were detected in tumor tissues of DDTC-Cu(I)-treated group. Our data indicates that DDTC-Cu(I) is an effective proteasome activity inhibitor with the potential to be explored as a drug for pancreatic cancer.

[139]

TÍTULO / TITLE: - A Differential MicroRNA Profile Distinguishes Cholangiocarcinoma from Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Sep 18.

●● [Enlace al texto completo \(gratis o de pago\) 1245/s10434-013-3240-y](#)

AUTORES / AUTHORS: - Collins AL; Wojcik S; Liu J; Frankel WL; Alder H; Yu L; Schmittgen TD; Croce CM; Bloomston M

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The Ohio State University, Columbus, OH, USA.

RESUMEN / SUMMARY: - BACKGROUND: Cancers of the bile duct and the pancreas are virtually indistinguishable using conventional histopathological and clinical characteristics. We sought to use microRNA (miR) profiling to differentiate these two cancers. METHODS: RNA was harvested from the tumors of patients undergoing curative resection for cholangiocarcinoma or pancreatic adenocarcinoma and compared with adjacent normal bile duct or pancreas, respectively. There were 31 pairs of cholangiocarcinoma with matched tumor and adjacent bile duct and nine pairs of pancreatic cancer with matched tumor and adjacent uninvolved pancreas that had sufficient quantity of RNA that were included in the final analysis. Differential microRNA expression profiles were determined using the nCounter System from nanoString Technologies (Seattle, WA, USA). RESULTS: A total of 41 differentially expressed miRs were identified in cholangiocarcinoma (25 overexpressed, 16 underexpressed) and 52 differentially expressed miRs were found in pancreatic adenocarcinoma (30 overexpressed, 22 underexpressed) relative to adjacent normal tissue. Of these two profiles, 15 miRs were commonly dysregulated between tumor types. Also, eight miRs were similarly overexpressed or underexpressed in cholangiocarcinoma and pancreatic adenocarcinoma, whereas the other seven miRs had inverse expression levels. CONCLUSIONS: Cholangiocarcinoma has a distinct miR profile from pancreatic adenocarcinoma. Discrimination between these two tumor types may be possible with as few as seven miRs.

[140]

TÍTULO / TITLE: - Predicting Dysplasia and Invasive Carcinoma in Intraductal Papillary Mucinous Neoplasms of the Pancreas: Development of a Preoperative Nomogram.

RESUMEN / SUMMARY: -

ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=24046103

- Enlace al texto completo (gratis o de pago) 1245/s10434-013-3207-z

AUTORES / AUTHORS: - Correa-Gallego C; Do R; Lafemina J; Gonen M; D'Angelica MI; Dematteo RP; Fong Y; Kingham TP; Brennan MF; Jarnagin WR; Allen PJ

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

RESUMEN / SUMMARY: - **BACKGROUND:** Clinical decision making for patients with intraductal papillary mucinous neoplasms (IPMN) of the pancreas is challenging. Even with strict criteria for resection, most resected lesions lack high-grade dysplasia (HGD) or invasive carcinoma. **METHODS:** We evaluated patients who underwent resection of histologically confirmed IPMN and had preoperative imaging available for review. A hepatobiliary radiologist blinded to histopathologic subtype reviewed preoperative imaging and recorded cyst characteristics. Patients with mixed-type IPMN were grouped with main-duct lesions for this analysis. Based on an ordinal logistic regression model, we devised two independent nomograms to predict the findings of adenoma, high-grade dysplasia (HGD-CIS), and invasive carcinoma, separately in both main and branch-duct IPMN. Bootstrap validation was used to evaluate the performance of these models, and a concordance index was derived from this internal validation. **RESULTS:** There were 219 patients who met criteria for this study. Branch-duct IPMN (bdIPMN) comprised 56 % of the resected lesions. The proportion of HGD-CIS was 15 % for bdIPMN and 33 % for main-duct lesions (mdIPMN); $P = 0.003$. Invasive carcinoma was identified in 15 % of bdIPMN and 41 % of main-duct lesions ($P < 0.001$). On multivariate regression, patient gender, history of prior malignancy, presence of solid component, and weight loss were found to be significantly associated with the ordinal outcome for patients with mdIPMN and built into the nomogram (concordance index 0.74). For patients with bdIPMN weight loss, solid component, and lesion diameter were associated with the outcome; (concordance index 0.74). **CONCLUSION:** Based on the analysis of patients selected for resection, two nomograms were created that predict a patient's individual likelihood of harboring HGD or invasive malignancy in radiologically diagnosed IPMN. External validation is ongoing.

[141]

TÍTULO / TITLE: - Phase I dose escalation study of the PKC α inhibitor aurothiomalate for advanced non-small-cell lung cancer, ovarian cancer, and pancreatic cancer.

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

REVISTA / JOURNAL: - Anticancer Drugs. 2013 Nov;24(10):1079-83. doi: 10.1097/CAD.000000000000009.

- Enlace al texto completo (gratis o de pago)

1097/CAD.000000000000009

AUTORES / AUTHORS: - Mansfield AS; Fields AP; Jatoi A; Qi Y; Adjei AA; Erlichman C; Molina JR

INSTITUCIÓN / INSTITUTION: - aDepartment of Medical Oncology, Mayo Clinic, Rochester, Minnesota bDepartment of Cancer Biology, Mayo Clinic, Jacksonville, Florida cDepartment of Internal Medicine, Greater Baltimore Medical Center, Baltimore, Maryland dDepartment of Medicine, Roswell Park Cancer Institute, Buffalo, New York, USA.

RESUMEN / SUMMARY: - Protein kinase C iota (PKC ι) is overexpressed in non-small-cell lung cancer, ovarian, and pancreatic cancers, where it plays a critical role in oncogenesis. The gold compound aurothiomalate (ATM) has been shown to inhibit PKC ι signaling and exerts potent antitumor activity in preclinical models. We sought to determine the maximum tolerated dose (MTD) of ATM. We conducted a phase I dose escalation trial of ATM in patients with non-small-cell lung cancer, ovarian or pancreatic cancer. Patients received ATM intramuscularly weekly for three cycles (cycle duration 4 weeks) at 25, 50, or 75 mg in a 3+3 design. The dose was not escalated for individual patients. Blood samples were analyzed for elemental gold levels. Patients were evaluated every 4 weeks for toxicity and every 8 weeks for response. Fifteen patients were enrolled in this study. Six patients were treated at 25 mg, seven at 50 mg, and two at 75 mg. There was one dose-limiting toxicity at 25 mg (hypokalemia), one at 50 mg (urinary tract infection), and none at 75 mg. There were three grade 3 hematologic toxicities. The recommended MTD of ATM is 50 mg. Patients received treatment for a median of two cycles (range 1-3). There appeared to be a dose-related accumulation of steady-state plasma concentrations of gold consistent with linear pharmacokinetics. In summary, this phase I study was successful in identifying ATM 50 mg intramuscularly weekly as the MTD. Future clinical investigations targeting PKC ι are currently in progress.

[142]

TÍTULO / TITLE: - Update on the management of gastroenteropancreatic neuroendocrine tumors with emphasis on the role of imaging.

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

REVISTA / JOURNAL: - AJR Am J Roentgenol. 2013 Oct;201(4):811-24. doi: 10.2214/AJR.12.10240.

●● Enlace al texto completo (gratis o de pago) [2214/AJR.12.10240](#)

AUTORES / AUTHORS: - Kim KW; Krajewski KM; Nishino M; Jagannathan JP; Shinagare AB; Tirumani SH; Ramaiya NH

INSTITUCIÓN / INSTITUTION: - 1 Department of Radiology, Dana-Farber Cancer Institute, 450 Brookline Ave, Boston, MA 02115.

RESUMEN / SUMMARY: - OBJECTIVE. The purposes of this article are to review the current management of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

based on the 2012 National Comprehensive Cancer Network guidelines and to describe the role of imaging in a multidisciplinary approach. CONCLUSION. The management of GEP-NETs has become complex, requiring a multidisciplinary approach. The World Health Organization classification of GEP-NETs has been revised; the U.S. Food and Drug Administration has approved molecular targeted agents (sunitinib, everolimus) for the treatment of pancreatic NETs; and the National Comprehensive Cancer Network clinical practice guidelines have been updated.

[143]

TÍTULO / TITLE: - HDLs protect the MIN6 insulinoma cell line against tunicamycin-induced apoptosis without inhibiting ER stress and without restoring ER functionality.

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

REVISTA / JOURNAL: - Mol Cell Endocrinol. 2013 Aug 28;381(1-2):291-301. doi: 10.1016/j.mce.2013.08.016.

●● Enlace al texto completo (gratis o de pago) [1016/j.mce.2013.08.016](#)

AUTORES / AUTHORS: - Puyal J; Petremand J; Dubuis G; Rummel C; Widmann C

INSTITUCIÓN / INSTITUTION: - Department of Fundamental Neurosciences, University of Lausanne, Switzerland.

RESUMEN / SUMMARY: - HDLs protect pancreatic beta cells against apoptosis induced by several endoplasmic reticulum (ER) stressors, including thapsigargin, cyclopiazonic acid, palmitate and insulin over-expression. This protection is mediated by the capacity of HDLs to maintain proper ER morphology and ER functions such as protein folding and trafficking. Here, we identified a distinct mode of protection exerted by HDLs in beta cells challenged with tunicamycin™, a protein glycosylation inhibitor inducing ER stress. HDLs were found to inhibit apoptosis induced by TM in the MIN6 insulinoma cell line and this correlated with the maintenance of a normal ER morphology. Surprisingly however, this protective response was neither associated with a significant ER stress reduction, nor with restoration of protein folding and trafficking in the ER. These data indicate that HDLs can use at least two mechanisms to protect beta cells against ER stressors. One that relies on the maintenance of ER function and one that operates independently of ER function modulation. The capacity of HDLs to activate several anti-apoptotic pathways in beta cells may explain their ability to efficiently protect these cells against a variety of insults.

[144]

TÍTULO / TITLE: - Expression of MUC4 Mucin Is Observed Mainly in the Intestinal Type of Intraductal Papillary Mucinous Neoplasm of the Pancreas.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1120-1128.

- Enlace al texto completo (gratis o de pago)

[1097/MPA.0b013e3182965915](https://doi.org/10.1007/MPA.0b013e3182965915)

AUTORES / AUTHORS: - Kitazono I; Higashi M; Kitamoto S; Yokoyama S; Horinouchi M; Osako M; Shimizu T; Tabata M; Batra SK; Goto M; Yonezawa S

INSTITUCIÓN / INSTITUTION: - From the *Department of Human Pathology, Field of Oncology, and daggerCardiovascular and Gastroenterological Surgery, Graduate School of Medical and Dental Sciences, Kagoshima University; double daggerDepartment of Pathology, and section signDepartment of Surgery, Kagoshima-shi Medical Association Hospital, Kagoshima, Japan; parallelDepartments of Biochemistry and Molecular Biology, Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, NE; and paragraph signNational Sanatorium Hoshizuka-Keiaien, Kanoya, Kagoshima, Japan.

RESUMEN / SUMMARY: - **OBJECTIVES:** This study aimed to examine expression profile of MUC4 in intraductal papillary mucinous neoplasm of the pancreas (IPMN). **METHODS:** We performed immunohistochemistry (IHC) of MUC4 in 142 IPMNs, with evaluation of the specificity of 2 anti-MUC4 monoclonal antibodies, 8G7 and 1G8, in cancer cell lines. **RESULTS:** Monoclonal antibody 8G7 showed a clear immunoreactivity, whereas MAb 1G8 did not show any immunoreactivity, in the Western blotting and IHC for human pancreatic carcinoma cell lines expressing MUC4 messenger RNA. However, IHC signals detected by both monoclonal antibodies were observed in the tissue specimens. The expression rates of MUC4/8G7 detected by MAb 8G7 and MUC4/1G8 detected by MAb 1G8 in the intestinal-type IPMNs were significantly higher than those in the gastric-type IPMNs. In the intestinal-type IPMNs, MUC4/8G7 was expressed mainly in the cytoplasm of the neoplastic cells, whereas MUC4/1G8 was expressed mainly at the cell apices. Even in the gastric-type IPMNs with rare MUC4 expression in the low-grade dysplasia, both MUC4 expression rates increased when dysplasia advanced. **CONCLUSIONS:** A significantly higher expression of MUC4 in intestinal-type IPMNs than in gastric-type IPMNs will be one of the biomarkers to discriminate between the intestinal-type IPMNs with high malignancy potential from gastric-type IPMNs with low malignancy potential.

[145]

TÍTULO / TITLE: - Elevated expression of tumor miR-222 in pancreatic cancer is associated with Ki67 and poor prognosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](https://doi.org/10.1007/s12032-013-0700-y)

REVISTA / JOURNAL: - Med Oncol. 2013 Dec;30(4):700. doi: 10.1007/s12032-013-0700-y. Epub 2013 Sep 13.

- Enlace al texto completo (gratis o de pago) [1007/s12032-013-0700-y](https://doi.org/10.1007/s12032-013-0700-y)

AUTORES / AUTHORS: - Lee C; He H; Jiang Y; Di Y; Yang F; Li J; Jin C; Fu D

INSTITUCIÓN / INSTITUTION: - Department of Pancreatic Surgery, Pancreatic Disease Institute, Huashan Hospital affiliated to Fudan University, No 12, WuRuWuQi Middle Road, Shanghai, 200040, China.

RESUMEN / SUMMARY: - Pancreatic cancer is known for its bad prognosis. Micro-RNAs mis-expressions are associated with various human cancers and offer new candidate targets for diagnostic and therapeutic strategies. Micro-RNA-222 has been shown to play a crucial role in cancer cell proliferation in recent studies. However, its correlations with the clinicopathological characters of pancreatic cancer still remain unclear. Through a prospective study of 60 pairs of pancreatic cancer tissues, adjacent normal tissues were examined by quantitative reverse-transcription polymerase chain reaction. The correlation between the expression of micro-RNA-222 and clinicopathological characters was performed using the two-sample Student's t test. The survival correlations were analyzed by the Kaplan-Meier method and the Cox's proportional hazards model. Results showed that the expression levels of micro-RNA-222 were significantly elevated in the pancreatic cancer tissue compared with that in adjacent normal tissue. In addition, the overexpression of the tissue micro-RNA-222 strongly related to the expression level of Ki67. Finally, Cox's proportional hazards model analysis confirmed that micro-RNA-222 high expression level was an independent predictor of poor prognosis. This study provides the first evidence of a potential link between Ki67 and micro-RNA-222, which are both relevant to cell proliferation. Our data suggest the potential of micro-RNA-222 as a prognostic biomarker for the pancreatic cancer.

[146]

TÍTULO / TITLE: - Annexin A10 is an immunohistochemical marker for adenocarcinoma of the upper gastrointestinal tract and pancreatobiliary system.

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

REVISTA / JOURNAL: - Histopathology. 2013 Jul 16. doi: 10.1111/his.12229.

●● [Enlace al texto completo \(gratis o de pago\) 1111/his.12229](#)

AUTORES / AUTHORS: - Lu SH; Yuan RH; Chen YL; Hsu HC; Jeng YM

INSTITUCIÓN / INSTITUTION: - Graduate Institute of Pathology, National Taiwan University, Taipei, Taiwan.

RESUMEN / SUMMARY: - AIMS: Annexin A10 (ANXA10) is a calcium- and phospholipid-binding protein expressed normally in the gastric mucosa. In this study, we evaluated the potential use of ANXA10 as a diagnostic marker. METHODS AND RESULTS: We observed ANXA10 expression in the gastric mucosa, the Brunner gland of the duodenum and the urothelium, but absence of expression in other normal organs. Following the screening of 1327 primary carcinomas of major organs, we identified ANXA10 expression in 46% of gastric, 72% of ampullary, 78% of pancreatic and 33% of biliary adenocarcinomas. ANXA10 was expressed in 83% of non-invasive urothelial

carcinomas, but was expressed in only 9% of invasive urothelial carcinomas. ANAX10 was rarely expressed in carcinomas of other organs. Of 227 metastatic adenocarcinomas, ANXA10 was expressed in 83% of metastatic pancreatic and 47% of metastatic gastric adenocarcinomas, but was expressed in only 2% of metastatic adenocarcinomas from other organs. In the liver, the sensitivity and specificity for identifying the pancreas as the primary site of metastatic adenocarcinoma were 83 and 95%, respectively. CONCLUSION: Our study results indicate that the inclusion of ANXA10 in an immunohistochemical panel will be helpful in the differential diagnosis of adenocarcinoma of an unknown primary site.

[147]

TÍTULO / TITLE: - Pancreatoblastoma: a rare, adult pancreatic tumor with many faces.

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

REVISTA / JOURNAL: - Arch Pathol Lab Med. 2013 Sep;137(9):1224-6. doi: 10.5858/arpa.2013-0272-CR.

●● Enlace al texto completo (gratis o de pago) [5858/arpa.2013-0272-CR](#)

AUTORES / AUTHORS: - Hammer ST; Owens SR

INSTITUCIÓN / INSTITUTION: - From the Department of Pathology, University of Michigan, Ann Arbor.

RESUMEN / SUMMARY: - Pancreatoblastomas are malignant epithelial neoplasms of the pancreas that are heterogeneous and have variable cellular differentiation, complicating the diagnosis. We report a case of pancreatoblastoma occurring in an adult patient, presenting as a pancreatic head mass with liver metastasis and jaundice. The initial liver biopsy diagnosis was metastatic neuroendocrine carcinoma based on morphology and synaptophysin positivity. At pancreatic resection, the diagnostic features of pancreatoblastoma were recognized. We review the radiologic and pathologic differential diagnosis, histologic heterogeneity, clinical presentation, and associated genetic syndromes for this unusual tumor that can mimic other types of pancreatic neoplasia.

[148]

TÍTULO / TITLE: - Planned versus unplanned portal vein resections during pancreaticoduodenectomy for adenocarcinoma.

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

REVISTA / JOURNAL: - Br J Surg. 2013 Sep;100(10):1349-56. doi: 10.1002/bjs.9222.

●● Enlace al texto completo (gratis o de pago) [1002/bjs.9222](#)

AUTORES / AUTHORS: - Kim PT; Wei AC; Atenafu EG; Cavallucci D; Cleary SP; Moulton CA; Greig PD; Gallinger S; Serra S; McGilvray ID

INSTITUCIÓN / INSTITUTION: - Hepatopancreatobiliary Surgical Oncology, Princess Margaret Cancer Center, University Health Network, University of Toronto, Toronto, Ontario, Canada.

RESUMEN / SUMMARY: - BACKGROUND: The management of portal vein (PV) involvement by pancreatic adenocarcinoma during pancreaticoduodenectomy (PD) is controversial. The aim of this study was to compare the outcomes of unplanned and planned PV resections as part of PD. METHODS: An analysis of PD over 11 years was performed. Patients who had undergone PV resection (PV-PD) were identified, and categorized into those who had undergone planned or unplanned resection. Postoperative and oncological outcomes were compared. RESULTS: Of 249 patients who underwent PD for pancreatic adenocarcinoma, 66 (26.5 per cent) had PV-PD, including 27 (41 per cent) planned and 39 (59 per cent) unplanned PV resections. Twenty-five of 27 planned PV resections were circumferential PV-PD, whereas 25 of 39 unplanned PV resections were partial PV-PD. Planned PV resections were performed in slightly younger patients (mean(s.d.) 60(9) versus 65(10) years; P = 0.031), and associated with longer operating times (mean(s.d.) 602(131) versus 458(83) min; P < 0.001) and more major complications (26 versus 5 per cent; P = 0.026). Planned PV resections were associated with a lower rate of positive margins (4 versus 44 per cent; P < 0.001) despite being carried out for larger tumours (mean(s.d.) 3.9(1.4) versus 2.9(1.0) cm; P = 0.002). There was no difference in survival between the two groups (P = 0.998). On multivariable analysis, margin status was a significant predictor of survival. CONCLUSION: Although planned PV resections for pancreatic adenocarcinoma were associated with higher rates of postoperative morbidity than unplanned resections, R0 resection rates were better.

[149]

TÍTULO / TITLE: - Resection of pancreatic tumors involving the anterior surface of the superior mesenteric/portal veins axis: an alternative procedure to pancreaticoduodenectomy with vein resection.

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

REVISTA / JOURNAL: - J Am Coll Surg. 2013 Oct;217(4):e21-8. doi: 10.1016/j.jamcollsurg.2013.07.383.

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

1016/j.jamcollsurg.2013.07.383

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INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliopancreatic Surgery, West China Hospital, Sichuan University, Chengdu, China.

[150]

TÍTULO / TITLE: - A Safe Technique for Radical Antegrade Modular Pancreatosplenectomy with Venous Resection for Pancreatic Cancer.

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

REVISTA / JOURNAL: - J Am Coll Surg. 2013 Sep 14. pii: S1072-7515(13)01025-9. doi: 10.1016/j.jamcollsurg.2013.08.007.

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

[1016/j.jamcollsurg.2013.08.007](#)

AUTORES / AUTHORS: - Rosso E; Langella S; Addeo P; Nobili C; Oussoultzoglou E; Jaeck D; Bachellier P

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[151]

TÍTULO / TITLE: - Pulsed high-intensity focused ultrasound enhances apoptosis of pancreatic cancer xenograft with gemcitabine.

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

REVISTA / JOURNAL: - Ultrasound Med Biol. 2013 Nov;39(11):1991-2000. doi: 10.1016/j.ultrasmedbio.2013.06.004. Epub 2013 Aug 22.

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

[1016/j.ultrasmedbio.2013.06.004](#)

AUTORES / AUTHORS: - Lee ES; Lee JY; Kim H; Choi Y; Park J; Han JK; Choi BI

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Seoul National University Hospital, Seoul, Korea.

RESUMEN / SUMMARY: - We sought to investigate whether concurrent exposure to pulsed high-intensity focused ultrasound (HIFU) and the chemotherapeutic drug gemcitabine would enhance apoptosis in pancreatic cancer. A pancreatic cancer xenograft model was established using BALB/c nude mice and human pancreatic cancer cells (PANC-1). In the first study, mice were randomly allocated into one of four groups: control (n = 4), HIFU alone (n = 4), gemcitabine (GEM) alone (n = 28) and concurrent treatment with HIFU and gemcitabine (HIGEM) (n = 28). The GEM and HIGEM groups were subdivided into four subgroups (16 mice) according to the drug dose injected (50-200 mg/kg) and another four subgroups (16 mice) according to the time interval between drug injection and HIFU treatment (each subgroup, n = 4). Apoptosis rates were evaluated using the TUNEL (terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling) assay and percentage of necrosis, as evaluated with Harris' hematoxylin solution and eosin Y stain, 3 d after treatment. The second study was performed to evaluate tumor growth rates of the four groups. Each group was treated weekly for 3 wk, and tumor size was periodically measured for up to

4 wk from the beginning of treatment. In the first study, overall rates of apoptosis were significantly higher in the HIGEM group than in the GEM group ($p = 0.02$). In a subgroup analysis, HIGEM was superior to GEM in enhancing apoptosis at gemcitabine dosages of 150-200 mg/kg gemcitabine and intervals between gemcitabine and HIFU less than 2 h ($p = 0.01$). In the second study, HIGEM treatment resulted in the slowest tumor growth. However, despite a visible distinction, none of the differences found between the HIGEM and GEM groups were statistically significant ($p > 0.05$). Treatment with both HIFU and gemcitabine might enhance cell apoptosis and reduce tumor growth in pancreatic carcinoma. For this concurrent treatment, a high dosage of gemcitabine and a short-term delay before HIFU are recommended to maximize the therapeutic effect.

[152]

TÍTULO / TITLE: - Outcomes with FOLFIRINOX for borderline resectable and locally unresectable pancreatic cancer.

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

REVISTA / JOURNAL: - J Surg Oncol. 2013 Sep;108(4):236-41. doi: 10.1002/jso.23392.

●● Enlace al texto completo (gratis o de pago) [1002/jso.23392](#)

AUTORES / AUTHORS: - Boone BA; Steve J; Krasinskas AM; Zureikat AH; Lembersky BC; Gibson MK; Stoller RG; Zeh HJ; Bahary N

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania.

RESUMEN / SUMMARY: - BACKGROUND: Trials examining FOLFIRINOX in metastatic pancreatic cancer demonstrate higher response rates compared to gemcitabine-based regimens. There is currently limited experience with neoadjuvant FOLFIRINOX in pancreatic cancer. METHODS: Retrospective review of outcomes of patients with borderline resectable or locally unresectable pancreatic cancer who were recommended to undergo neoadjuvant treatment with FOLFIRINOX. RESULTS: FOLFIRINOX was recommended for 25 patients with pancreatic cancer, 13 (52%) unresectable and 12 (48%) borderline resectable. Four patients (16%) refused treatment or were lost to follow-up. Twenty-one patients (84%) were treated with a median of 4.7 cycles. Six patients (29%) required dose reductions secondary to toxicity. Two patients (9%) were unable to tolerate treatment and three patients (14%) had disease progression on treatment. Seven patients (33%) underwent surgical resection following treatment with FOLFIRINOX alone, 2 (10%) of which were initially unresectable. Two patients underwent resection following FOLFIRINOX + stereotactic body radiation therapy (SBRT). The R0 resection rate for patients treated with FOLFIRINOX +/- SBRT was 33% (55% borderline resectable, 10% unresectable). A total of five patients (24%) demonstrated a significant pathologic response. CONCLUSIONS: FOLFIRINOX is a biologically active regimen in borderline resectable and locally

unresectable pancreatic cancer with encouraging R0 resection and pathologic response rates. J. Surg. Oncol. 2013 108:236-241. © 2013 Wiley Periodicals, Inc.

[153]

TÍTULO / TITLE: - Aberrant Expression of CXCR4 and beta-Catenin in Pancreatic Cancer.

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

REVISTA / JOURNAL: - Anticancer Res. 2013 Sep;33(9):4103-10.

AUTORES / AUTHORS: - Wang Z; Ma Q; Li P; Sha H; Li X; Xu J

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, The First Affiliated Hospital, Medical College of Xi'an Jiaotong University, Xi'an 710061, Shaanxi, P.R. China. gyma56@mail.xjtu.edu.cn or xjxpx@189.cn.

RESUMEN / SUMMARY: - Aim: The stromal cell-derived factor-1 (SDF-1)/C-X-C chemokine receptor type 4 (CXCR4) axis and Wingless and INT-1 (Wnt)/beta-catenin pathway has been related to cancer progression. The aim of this study was to investigate the expression of CXCR4 and beta-catenin in pancreatic cancer. PATIENTS AND METHODS: A total of 48 pancreatic cancer samples and 8 normal pancreatic tissues were selected to detect CXCR4 and beta-catenin expression by an immunohistological technique. Spearman and Chi-square analyses were used to study the relation between the protein expression and clinical characteristics. Survival analysis was evaluated by the Kaplan-Meier product limit method. RESULTS: The proportions of CXCR4 and beta-catenin expression on pancreatic cancer cells were significantly higher than in normal pancreas tissues. There was a significant difference in CXCR4 expression levels, lymph node metastasis and TNM stage. Clinical Significance was observed for beta-catenin expression and lymph node metastasis; Kaplan-Meier curves suggested that clinical prognosis is poor for patients expressing CXCR4. Multivariate analysis showed that CXCR4 expression was an independent prognostic factor for pancreatic cancer. CONCLUSION: Both CXCR4 and beta-catenin are abnormally expressed in pancreatic cancer. CXCR4 may be an important marker for pancreatic cancer progression.

[154]

TÍTULO / TITLE: - Microwave ablation of pancreatic head cancer: safety and efficacy.

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

REVISTA / JOURNAL: - J Vasc Interv Radiol. 2013 Oct;24(10):1513-20. doi: 10.1016/j.jvir.2013.07.005.

●● Enlace al texto completo (gratis o de pago) [1016/j.jvir.2013.07.005](https://doi.org/10.1016/j.jvir.2013.07.005)

AUTORES / AUTHORS: - Carrafiello G; Ierardi AM; Fontana F; Petrillo M; Floridi C; Lucchina N; Cuffari S; Dionigi G; Rotondo A; Fugazzola C

INSTITUCIÓN / INSTITUTION: - Division of Interventional Radiology, Department of Radiology, University of Insubria, Varese, Italy. Electronic address: gcarraf@gmail.com.

RESUMEN / SUMMARY: - PURPOSE: To evaluate the safety and efficacy of percutaneous microwave (MW) ablation treatment in locally advanced, nonresectable, nonmetastatic pancreatic head cancer. MATERIALS AND METHODS: Ten patients with pancreatic head cancer treated with percutaneous (n = 5) or laparotomic (n = 5) MW ablation were retrospectively reviewed. The MW generator used (45 W at 915 MHz) was connected by coaxial cable to 14-gauge straight MW antennas with a 3.7- or 2-cm radiating section. One or two antennae were used, with an ablation time of 10 minutes. Ultrasonographic (US) and combined US/cone-beam computed tomographic (CT) guidance were used in five patients each. Follow-up was performed by CT after 1, 3, 6, and, when possible, 12 months. Tumor response was assessed per Response Evaluation Criteria In Solid Tumors (version 1.1) and Choi criteria. The feasibility, safety, and major and minor complications associated with quality of life (QOL) were recorded prospectively. RESULTS: The procedure was feasible in all patients (100%). One late major complication was observed in one patient, and no visceral injury was detected. No patient had further surgery, and all minor complications resolved during the hospital stay. An improvement in QOL was observed in all patients despite a tendency to return to preoperative levels in the months following the procedure, without the influence of minor complications. No repeat treatment was performed. CONCLUSIONS: Despite the small number of patients, the present results can be considered encouraging, showing that MW ablation is a feasible approach in the palliative treatment of pancreatic tumors.

[155]

TÍTULO / TITLE: - Contrast-enhanced multiphasic CT and MRI findings of adenosquamous carcinoma of the pancreas.

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

REVISTA / JOURNAL: - Clin Imaging. 2013 Sep 10. pii: S0899-7071(13)00190-3. doi: 10.1016/j.clinimag.2013.08.002.

●● Enlace al texto completo (gratis o de pago) [1016/j.clinimag.2013.08.002](#)

AUTORES / AUTHORS: - Ding Y; Zhou J; Sun H; He D; Zeng M; Rao S

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Zhongshan Hospital, Fudan University and Shanghai Medical Imaging, Institute, Shanghai 200032, People's Republic of China; Department of Medical Imaging, Shanghai Medical School of Fudan University, Shanghai, 200032, People's Republic of China.

RESUMEN / SUMMARY: - OBJECTIVE: The objective was to retrospectively study computed tomography (CT) and magnetic resonance imaging (MRI) findings of adenosquamous carcinoma of the pancreas (PASC). MATERIALS AND METHODS: Twelve patients (six women and six men; mean age, 61.3 years; range, 47-78 years) who presented with PASC as documented by pathologic examination underwent CT (n=10) or both CT and MRI (n=2) examination. Two radiologists evaluated the images

and determined the location, size, margin, internal attenuation or signal intensity, contrast enhancement, and pattern for each tumor. Additionally, the presence of poorly enhanced areas, upstream main pancreatic duct (MPD) dilatation, pancreatic atrophy, and peripancreatic tissue metastasis were evaluated. Images were cross-referenced to surgical and pathologic findings. RESULTS: Masses were distributed throughout the pancreas (head, n=6; body, n=1; and tail, n=5). The tumor size ranged from 2.4 to 5.5 cm with an average size of 3.7 cm. Eight (66.7%) masses were ill defined, and seven (58.3%) were partially exophytic. Twelve (100%) masses showed heterogeneous and poorly enhanced areas. The lesions showed weak (n=5), moderate (n=5), or intense (n=2) progressive enhancement. The diameter of MPD in six patients ranged from 3.0 to 5.0 mm with an average of 3.7 mm. Pancreatic atrophy was not found. In 10 patients (83.3%), masses invaded the peripancreatic tissues. Two patients had metastatic liver disease at presentation. CONCLUSION: PASC typically presented as an ill-defined, hypovascular mass with a poorly enhanced area, exophytic tendency, and peripancreatic tissue invasion. Lack of pancreatic atrophy and mild MPD dilatation were also distinct from common duct pancreatic adenocarcinoma.

[156]

TÍTULO / TITLE: - Pancreatic actinomycosis presenting as pancreatic mass and diagnosed with endoscopic ultrasound fine needle aspiration (EUS-FNA).

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

REVISTA / JOURNAL: - Endoscopy. 2013 Sep;45 Suppl 2:E276-7. doi: 10.1055/s-0032-1310142. Epub 2013 Sep 5.

●● Enlace al texto completo (gratis o de pago) [1055/s-0032-1310142](#)

AUTORES / AUTHORS: - Maestro S; Trujillo R; Geneux K; Garcia M; Martinez A; Millan AG; Arisqueta F

INSTITUCIÓN / INSTITUTION: - Hospital Rio Carrion-Digestivo, Palencia, Palencia, España.

[157]

TÍTULO / TITLE: - Gastroenteropancreatic endocrine tumors.

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

REVISTA / JOURNAL: - Mol Cell Endocrinol. 2013 Jul 30. pii: S0303-7207(13)00309-2. doi: 10.1016/j.mce.2013.07.015.

●● Enlace al texto completo (gratis o de pago) [1016/j.mce.2013.07.015](#)

AUTORES / AUTHORS: - Meeker A; Heaphy C

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ameeker1@jhmi.edu.

RESUMEN / SUMMARY: - Gastroenteropancreatic endocrine tumors (GEP-NETs) are relatively uncommon; comprising approximately 0.5% of all human cancers. Although they often exhibit relatively indolent clinical courses, GEP-NETs have the potential for lethal progression. Due to their scarcity and various technical challenges, GEP-NETs have been understudied. As a consequence, we have few diagnostic, prognostic and predictive biomarkers for these tumors. Early detection and surgical removal is currently the only reliable curative treatment for GEP-NET patients; many of whom, unfortunately, present with advanced disease. Here, we review the genetics and epigenetics of GEP-NETs. The last few years have witnessed unprecedented technological advances in these fields, and their application to GEP-NETS has already led to important new information on the molecular abnormalities underlying them. As outlined here, we expect that “omics” studies will provide us with new diagnostic and prognostic biomarkers, inform the development of improved pre-clinical models, and identify novel therapeutic targets for GEP-NET patients.

[158]

TÍTULO / TITLE: - Biomarkers for pancreatic cancer: promising new markers and options beyond CA 19-9.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Aug 17.

- [Enlace al texto completo \(gratis o de pago\) 1007/s13277-013-1033-3](#)

AUTORES / AUTHORS: - Ballehaninna UK; Chamberlain RS

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Saint Barnabas Medical Center, 94, Old Short Hills Road, Livingston, NJ, 07039, USA.

RESUMEN / SUMMARY: - Pancreatic adenocarcinoma accounts for nearly 90-95 % of exocrine malignant tumors of the pancreas. Traditionally, overexpressed proteins/epitopes such as CA 19-9, CA-50, CEA, and many others were being used as pancreatic cancer tumor markers. The main utility of these biomarkers was in the diagnosis of pancreatic cancer as well as to assess response to chemotherapy and to determine prognosis and to predict tumor recurrence. However, these markers had significant limitations such as lack of sensitivity, false-negative results in certain blood groups, as well as false-positive elevation in the presence of obstructive jaundice. To circumvent these limitations, an extraordinary amount of research is being performed to identify an accurate tumor marker or a panel of markers that could aid in the management of the pancreatic cancer. Although this research has identified a large number and different variety of biomarkers, few hold future promise as a preferred marker for pancreatic cancer. This review provides an insight into exciting new areas of pancreatic biomarker research such as salivary, pancreatic juice, and stool markers that can be used as a noninvasive test to identify pancreatic cancer. This manuscript also provides a discussion on newer biomarkers, the role of microRNAs, and pancreatic

cancer proteomics, which have the potential to identify a preferred tumor marker for pancreatic adenocarcinoma. This review further elaborates on important genetic changes associated with the development and progression of pancreatic cancer that holds the key for the identification of a sensitive biomarker and which could also serve as a therapeutic target.

[159]

TÍTULO / TITLE: - Infantile Extrapancreatic Pancreatoblastoma: A Report on a Rare Infantile Abdominal Mass.

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

REVISTA / JOURNAL: - J Pediatr Hematol Oncol. 2013 Sep 25.

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

[1097/MPH.0b013e3182a0627f](#)

AUTORES / AUTHORS: - Esfahani H; Olad E; Dehghan A; Bazmamoun H; Ghorbanpoor M

INSTITUCIÓN / INSTITUTION: - Departments of *Pediatric Hematology/Oncology
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Hamadan University of Medical Science, Hamadan, Islamic Republic of Iran.

RESUMEN / SUMMARY: - Pancreatoblastoma is an extremely rare tumor in children, especially under 3 months of age. This tumor may arise from any portion of the pancreas, but in more rare cases the ectopic pancreas is the origin. We are reporting a 3-month-old boy who was presented with an abdominal mass. Computed tomography images revealed a huge lobulated mass anterior to the kidneys, with internal calcification and enhancement after intravenous contrast media injection. He underwent a complete surgical resection of the mass that was located in the transverse mesocolon without any connection with the pancreas. Pathologic studies specified that the disease was pancreatoblastoma. His parents refused any chemotherapeutic regimen but continued postsurgical follow-ups.

[160]

TÍTULO / TITLE: - MiR-148^a regulates the growth and apoptosis in pancreatic cancer by targeting CCKBR and Bcl-2.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Aug 23.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1115-2](#)

AUTORES / AUTHORS: - Zhang R; Li M; Zang W; Wang Y; Li P; Du Y; Zhao G; Li L

INSTITUCIÓN / INSTITUTION: - Department of Emergency, The First Affiliated Hospital of Zhengzhou University, No. 1 Jianshe Road, Zhengzhou, Henan, 450052, China.

RESUMEN / SUMMARY: - Our previous studies have revealed that miR-148^a is downregulated in pancreatic cancer. Bioinformatics analysis has shown

cholecystikinin-B receptor (CCKBR) and B cell lymphoma (Bcl-2) to be potential targets of miR-148^a. But the pathophysiologic role of miR-148^a and its relevance to the growth and development of pancreatic cancer are yet to be investigated. The purpose of this study is to elucidate the molecular mechanisms where miR-148^a acts as a tumor suppressor in pancreatic cancer. Our results showed significant downregulation of miR-148^a in 28 pancreatic cancer tissue samples and five pancreatic cancer cell lines, compared with their non-tumor counterparts by qRT-PCR. MiR-148^a was found to not only inhibit the proliferation of pancreatic cancer cells (PANC-1 and AsPC-1) in vitro by MTT assay and colony formation assay, but also to promote cells apoptosis in vitro by Annexin V-FITC apoptosis detection and caspase activity assay. Using western blot and luciferase activity assay, CCKBR and Bcl-2 were identified as targets of miR-148^a. Moreover, we also found that the expression of Bcl-2 lacking in 3'UTR could abrogate the pro-apoptosis function of miR-148^a. These findings suggest the importance of miR-148^a's targeting of CCKBR and Bcl-2 in the regulation of pancreatic cancer growth and apoptosis.

[161]

TÍTULO / TITLE: - Lysophosphatidic Acid Stimulates Activation of Focal Adhesion Kinase and Paxillin and Promotes Cell Motility, via LPA1-3, in Human Pancreatic Cancer.

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

REVISTA / JOURNAL: - Dig Dis Sci. 2013 Sep 24.

●● Enlace al texto completo (gratis o de pago) [1007/s10620-013-2878-4](#)

AUTORES / AUTHORS: - Liao Y; Mu G; Zhang L; Zhou W; Zhang J; Yu H

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Renmin Hospital of Wuhan University, Number 238, Jiefang Road, Wuhan, 430060, Hubei Province, China, 13437145121@126.com.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is highly metastatic and with poor prognosis. In previous studies, lysophosphatidic acid (LPA) was shown to be a critical component of ascites which promoted the invasion and metastasis of pancreatic cancer. Two focal adhesion proteins, focal adhesion kinase (FAK) and paxillin, were crucially involved in cell migration, cytoskeleton reorganization, and the dynamics of focal adhesion. OBJECTIVES: This study examined the involvement of LPA1-3 in LPA-induced activation of FAK and paxillin, and in cell motility, in pancreatic cancer PANC-1 cells. METHODS: Reverse transcriptase polymerase chain reaction analysis was used to examine mRNA expression of LPA receptors in PANC-1. Cellular protein expression of FAK and paxillin was analyzed by western blotting. The subcellular location of FAK and paxillin was visualized by immunofluorescence. Cell migration was measured by use of a transwell migration chamber. RESULTS: Three LPA receptors (LPA1, LPA2, and LPA3) were significantly expressed in PANC-1 cells. Treatment with LPA induced both time and dose-dependent tyrosine phosphorylation

of FAK and paxillin. LPA also affected translocation of FAK and paxillin from cytoplasm to focal adhesions at the cell periphery and enhanced cell motility of PANC-1. Pretreatment with 3-(4-(4-((1-(2-chlorophenyl)ethoxy)carbonyl amino)-3-methyl-5-isoxazolyl)benzylsulfanyl)propanoic acid (Ki16425), an antagonist of LPA1 and LPA3, before LPA attenuated the LPA-induced tyrosine phosphorylation and redistribution of FAK and paxillin and abrogated LPA-induced cellular migration activity. CONCLUSIONS: These results suggest LPA induces activation of FAK and paxillin via LPA1-3, which may contribute to the increased cell motility in human pancreatic cancer PANC-1 cells. Thus, an understanding of the regulation by LPA of cell motility in pancreatic cancer could identify novel targets for therapy.

[162]

TÍTULO / TITLE: - Negative Impact of Fresh-frozen Plasma Transfusion on Prognosis of Pancreatic Ductal Adenocarcinoma After Pancreatic Resection.

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

REVISTA / JOURNAL: - Anticancer Res. 2013 Sep;33(9):4041-7.

AUTORES / AUTHORS: - Shiba H; Misawa T; Fujiwara Y; Futagawa Y; Furukawa K; Haruki K; Iida T; Iwase R; Yanaga K

INSTITUCIÓN / INSTITUTION: - Jikei University School of Medicine, 3-25-8, Nishi-Shinbashi, Minato-ku, Tokyo 105-8461, Japan. hs0817@jikei.ac.jp.

RESUMEN / SUMMARY: - BACKGROUND: Excessive blood loss and blood transfusion may influence postoperative complications and prognosis of patients after pancreatic resection. We evaluated the influence of blood products use on postoperative recurrence and outcome of patients with pancreatic ductal adenocarcinoma. PATIENTS AND METHODS: The study included 82 patients who underwent elective pancreatic resections for pancreatic ductal adenocarcinoma without distant metastasis or other malignancies between January 2001 and December 2010. We retrospectively investigated the influence of the use of perioperative blood products including red cell concentrate, fresh-frozen plasma (FFP), and albumin preparation, and clinical variables regarding disease-free and overall survival. RESULTS: In disease-free survival, serum carcinoembryonic antigen more than 10 ng/ml ($p=0.015$), serum carbohydrate antigen 19-9 (CA19-9) more than 200 U/ml ($p=0.0032$), R1 resection ($p=0.005$), and FFP transfusion were independent risk factors for cancer recurrence in the Cox proportional regression model, pancreaticoduodenectomy ($p=0.057$) and advanced tumor stage ($p=0.083$) tended to associate with poor disease-free survival, but were not statistically significant. In overall survival, male gender ($p=0.012$), advanced tumor stage ($p=0.005$), serum CA19-9 more than 200 U/ml ($p<0.001$), and FFP transfusion ($p=0.003$) were positively associated with poor overall survival in the Cox proportional regression model. CONCLUSION: FFP transfusion is associated with poor therapeutic outcome after elective pancreatic resection for pancreatic ductal adenocarcinoma.

[163]

TÍTULO / TITLE: - Dynamic computed tomography of locally advanced pancreatic cancer: effect of low tube voltage and a hybrid iterative reconstruction algorithm on image quality.

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

REVISTA / JOURNAL: - J Comput Assist Tomogr. 2013 Sep-Oct;37(5):790-6. doi: 10.1097/RCT.0b013e318296db2b.

●● Enlace al texto completo (gratis o de pago) [1097/RCT.0b013e318296db2b](#)

AUTORES / AUTHORS: - Yamamura S; Oda S; Utsunomiya D; Funama Y; Imuta M; Namimoto T; Hirai T; Chikamoto A; Baba H; Yamashita Y

INSTITUCIÓN / INSTITUTION: - From the Departments of *Diagnostic Radiology, daggerMedical Physics, and double daggerGastroenterological Surgery, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan.

RESUMEN / SUMMARY: - OBJECTIVE: The objective of this study was to evaluate the effect of a low-tube-voltage technique and hybrid iterative reconstruction (HIR) on image quality at dynamic computed tomography (CT) of the pancreas. METHODS: The study included 18 consecutive patients (10 women, 8 men; mean age, 68.5 +/- 9.5 years) with locally advanced pancreatic cancer who received chemotherapy and had stable disease during the 100- and 120-kV CT studies. The 120-kV images were reconstructed using filtered back projection, and the 100-kV images were postprocessed using filtered back projection and HIR. Scans obtained during 3 pancreatic phases were subjected to quantitative and qualitative analysis. RESULTS: The mean effective dose was significantly lower under the 100- than the 120-kV protocols (29.2 +/- 3.6 vs 52.1 +/- 5.1 mSv; P < 0.01). The mean contrast-to-noise ratio of the pancreatic cancer and the visual scores were significantly higher under 100 kV with HIR than those under the other 2 protocols (P < 0.01). CONCLUSIONS: Use of low tube voltage and HIR can provide significantly improved image quality at pancreatic dynamic CT.

[164]

TÍTULO / TITLE: - Metastases to the pancreas diagnosed by fine-needle aspiration.

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

REVISTA / JOURNAL: - Acta Cytol. 2013;57(5):473-80. doi: 10.1159/000352006. Epub 2013 Sep 7.

●● Enlace al texto completo (gratis o de pago) [1159/000352006](#)

AUTORES / AUTHORS: - Olson MT; Wakely PE Jr; Ali SZ

INSTITUCIÓN / INSTITUTION: - Department of Pathology, The Johns Hopkins Hospital, Baltimore, Md., USA.

RESUMEN / SUMMARY: - Background: Metastatic cancer infrequently involves the pancreas. When the pancreas hosts a metastatic tumor, cytopathological evaluation of fine-needle aspirate material is a crucial part of the diagnostic process. In this study, we show two institutions' experience with cytopathological diagnosis of pancreatic metastasis. Methods: Databases of institutional experience at The Johns Hopkins Hospital and Ohio State University Medical Center were queried for cases of metastatic tumors in the pancreas that underwent fine-needle aspiration. Demographic and pathological features were compiled and the cytomorphology was reviewed. Results: Forty-two cases of tumor metastasis to the pancreas were found. Over the time of this review, 5,495 aspirates were performed, and 43% (2,389/5,495) had malignant cytological findings. Thus, the 42 cases of metastatic disease to the pancreas comprised 0.8% of all pancreas aspirates and 1.8% of the malignant ones. Renal cell carcinoma was the most common metastasis, followed by melanoma and non-small cell lung carcinoma. Among the other tumors in this series, 2 cases each of rare metastases such as the fibrolamellar variant of hepatocellular carcinoma and solitary fibrous tumor were also seen. Conclusion: The pancreas is rarely involved with metastatic disease, but when it is involved the most common tumor is renal cell carcinoma followed by melanoma and non-small cell lung cancer. Clinical history and awareness of the primary pancreatic mimickers are necessary for arriving at the correct diagnosis. As conventional pancreatic adenocarcinoma is uncommon in children and young adults, history of other tumors - even ones that usually follow an indolent course - is essential. © 2013 S. Karger AG, Basel.

[165]

TÍTULO / TITLE: - Influences of the diabetes surgery on pancreatic beta-cells mass.

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

REVISTA / JOURNAL: - Nutr Hosp. 2013 Mar;28 Suppl 2:88-94. doi: 10.3305/nh.2013.28.sup2.6718.

●● [Enlace al texto completo \(gratis o de pago\) 3305/nh.2013.28.sup2.6718](#)

AUTORES / AUTHORS: - Martinez-Moreno JM; Garciacaballero M

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RESUMEN / SUMMARY: - In diabetes mellitus type 2 (DMT2), malfunction and apoptosis of beta-cell provoke a deficient insulin secretion. Generally, has been sustained that beta-cell function is severely compromised in type 2 diabetes before the disease appears and then continues to decrease linearly with time. Diversionary bariatric procedures such as gastric bypass, biliopancreatic diversion, one anastomosis gastric by-pass (BAGUA) and others that bypasses the foregut, induce a rapid non-weight-loss-associated improvement in glycemic control, especially if treated early before irreparable beta-cell damage has occurred. The antidiabetic effect of bariatric

operations is likely due to the improvement in the hormonal dysregulation associated with the development of diabetes. Now we know that the bariatric surgery through the reorganization of the gastrointestinal tract can affect to beta-cells mass homeostasis, stopped apoptosis and stimulate the replication and neogenesis. These effects are caused mainly by three stimuli: caloric restriction, rapid transit of food to the ileum and the exclusion of an intestinal portion including the stomach, duodenum and part of the jejunum. Several mechanisms have been proposed for this exciting effect that may provide key insights into the pathogenesis of type-2 diabetes. All of these mechanisms include from gut hormones such as ghrelin to second messengers such as AKT system or protein kinase B. Although not all the processes involved in the homeostasis of beta-cells are clear, we can explain some of the effects of bariatric surgery exerted on this important set of endocrine cells, which are essential in diabetes control.

[166]

TÍTULO / TITLE: - A Resected Perivascular Epithelioid Cell Tumor (PEComa) of the Pancreas Diagnosed Using Endoscopic Ultrasound-guided Fine-needle Aspiration.

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

REVISTA / JOURNAL: - Intern Med. 2013;52(18):2061-6.

AUTORES / AUTHORS: - Okuwaki K; Kida M; Masutani H; Yamauchi H; Katagiri H; Mikami T; Miyazawa S; Iwai T; Takezawa M; Imaizumi H; Koizumi W

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Kitasato University School of Medicine, Japan.

RESUMEN / SUMMARY: - Primary perivascular epithelioid cell tumors (PEComas) of the pancreas are extremely rare. We herein report our experience with a patient who had a primary PEComa of the pancreas that was diagnosed by the preoperative histopathological examination of a biopsy specimen obtained by endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). The patient was a 43-year-old woman whose chief complaint was abdominal pain. Imaging studies revealed a pancreatic tumor. Gastrointestinal stromal tumor (GIST), solid pseudopapillary tumor and neuroendocrine tumor were considered in the differential diagnosis. A histopathological examination of a specimen of the tumor obtained using EUS-FNA showed spindle-shaped tumor cells with enlarged nuclei and eosinophilic cytoplasm. The tumor cells proliferated in a sheet-like fashion and stained positive for the melanoma-associated antigen HMB-45. A PEComa was thus diagnosed. If an adequate tumor specimen can be obtained using EUS-FNA, immunostaining may facilitate the diagnosis of extremely rare diseases and therefore assist in deciding the treatment policy.

[167]

TÍTULO / TITLE: - Pancreatic paracoccidioidomycosis simulating malignant neoplasia: Case report.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Sep 14;19(34):5750-3. doi: 10.3748/wjg.v19.i34.5750.

●● [Enlace al texto completo \(gratis o de pago\) 3748/wjg.v19.i34.5750](#)

AUTORES / AUTHORS: - Lima TB; Domingues MA; Caramori CA; Silva GF; de Oliveira CV; Yamashiro Fda S; Franzoni Lde C; Sasaki LY; Romeiro FG

INSTITUCIÓN / INSTITUTION: - Talles Bazeia Lima, Carlos Antonio Caramori, Giovanni Faria Silva, Cassio Vieira de Oliveira, Fabio da Silva Yamashiro, Leticia de Campos Franzoni, Ligia Yukie Sasaki, Fernando Gomes Romeiro, Division of Gastroenterology, Department of Internal Medicine, Botucatu School of Medicine, Rubiao Junior District S/N, 18618-970 Sao Paulo, Brazil.

RESUMEN / SUMMARY: - Paracoccidioidomycosis is a systemic granulomatous disease caused by fungus, and must be considered in the differential diagnosis of intra-abdominal tumors in endemic areas. We report a rare case of paracoccidioidomycosis in the pancreas. A 45-year-old man was referred to our institution with a 2-mo history of epigastric abdominal pain that was not diet-related, with night sweating, inappetence, weight loss, jaundice, pruritus, choloria, and acholic feces, without signs of sepsis or palpable tumors. Abdominal ultrasonography (US) showed a solid mass of approximately 7 cm x 5.5 cm on the pancreas head. Abdominal computerized tomography showed dilation of the biliary tract, an enlarged pancreas (up to 4.5 in the head region), with dilation of the major pancreatic duct. The patient underwent exploratory laparotomy, and the surgical description consisted of a tumor, measuring 7 to 8 cm with a poorly-defined margin, adhering to posterior planes and mesenteric vessels, showing an enlarged bile duct. External drainage of the biliary tract, Roux-en-Y gastroenteroanastomosis, lymph node excision, and biopsies were performed, but malignant neoplasia was not found. Microscopic analysis showed chronic pancreatitis and a granulomatous chronic inflammatory process in the choledochal lymph node. Acid-alcohol resistant bacillus and fungus screening were negative. Fine-needle aspiration of the pancreas was performed under US guidance. The smear was compatible with infection by Paracoccidioides brasiliensis. We report a rare case of paracoccidioidomycosis simulating a malignant neoplasia in the pancreas head.

[168]

TÍTULO / TITLE: - Downregulation of gas5 increases pancreatic cancer cell proliferation by regulating CDK6.

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

REVISTA / JOURNAL: - Cell Tissue Res. 2013 Sep 12.

●● Enlace al texto completo (gratis o de pago) [1007/s00441-013-1711-x](https://doi.org/10.3748/wjg.v19.i28.4511)

AUTORES / AUTHORS: - Lu X; Fang Y; Wang Z; Xie J; Zhan Q; Deng X; Chen H; Jin J; Peng C; Li H; Shen B

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, RuiJin Hospital, Shanghai Jiaotong University School of Medicine, 197 RuiJin.Er.Road, ShangHai, 200025, China.

RESUMEN / SUMMARY: - Recent studies have revealed that long non-coding RNAs (lncRNAs) play important roles in cancer biology and that lncRNA gas5 (growth arrest-specific 5) regulates breast cancer cell growth. However, the role of gas5 in pancreatic cancer progression remains largely unknown. In the current study, we assay the expression level of gas5 in pancreatic cancer tissues and define the role of gas5 in the regulation of pancreatic cancer cell proliferation. We verify that the expression level of gas5 is significantly decreased in pancreatic cancer tissues compared with normal control. Overexpression of gas5 in pancreatic cancer cells inhibits cell proliferation, whereas gas5 inhibition induces a significant decrease in G0/G1 phase and an increase in S phase. We further demonstrate that gas5 negatively regulates CDK6 (cyclin-dependent kinase 6) expression in vitro and in vivo. More importantly, knockdown of CDK6 partially abrogates gas5-siRNA-induced cell proliferation. These data suggest an important role of gas5 in the molecular etiology of pancreatic cancer and implicate the potential application of gas5 in pancreatic cancer therapy.

[169]

TÍTULO / TITLE: - First-line erlotinib and fixed dose-rate gemcitabine for advanced pancreatic cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](https://doi.org/10.3748/wjg.v19.i28.4511)

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Jul 28;19(28):4511-9. doi: 10.3748/wjg.v19.i28.4511.

●● Enlace al texto completo (gratis o de pago) [3748/wjg.v19.i28.4511](https://doi.org/10.3748/wjg.v19.i28.4511)

AUTORES / AUTHORS: - Vaccaro V; Bria E; Sperduti I; Gelibter A; Moscetti L; Mansueto G; Ruggeri EM; Gamucci T; Cognetti F; Milella M

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Regina Elena National Cancer Institute, 00144 Rome, Italy.

RESUMEN / SUMMARY: - AIM: To investigate activity, toxicity, and prognostic factors for survival of erlotinib and fixed dose-rate gemcitabine (FDR-Gem) in advanced pancreatic cancer. METHODS: We designed a single-arm prospective, multicentre, open-label phase II study to evaluate the combination of erlotinib (100 mg/d, orally) and weekly FDR-Gem (1000 mg/m²), infused at 10 mg/m² per minute) in a population of previously untreated patients with locally advanced, inoperable, or metastatic pancreatic cancer. Primary endpoint was the rate of progression-free survival at 6 mo (PFS-6); secondary endpoints were overall response rate (ORR), response duration, tolerability, overall survival (OS), and clinical benefit. Treatment

was not considered to be of further interest if the PFS-6 was < 20% (p0 = 20%), while a PFS-6 > 40% would be of considerable interest (p1 = 40%); with a 5% rejection error (alpha = 5%) and a power of 80%, 35 fully evaluable patients with metastatic disease were required to be enrolled in order to complete the study. Analysis of prognostic factors for survival was also carried out. RESULTS: From May 2007 to September 2009, 46 patients were enrolled (male/female: 25/21; median age: 64 years; median baseline carbohydrate antigen 19-9 (CA 19-9): 897 U/mL; locally advanced/metastatic disease: 5/41). PFS-6 and median PFS were 30.4% and 14 wk (95%CI: 10-19), respectively; 1-year and median OS were 20.2% and 26 wk (95%CI: 8-43). Five patients achieved an objective response (ORR: 10.9%, 95%CI: 1.9-19.9); disease control rate was 56.5% (95%CI: 42.2-70.8); clinical benefit rate was 43.5% (95%CI: 29.1-57.8). CA 19-9 serum levels were decreased by > 25% as compared to baseline in 14/23 evaluable patients (63.6%). Treatment was well-tolerated, with skin rash being the most powerful predictor of both longer PFS (P < 0.0001) and OS (P = 0.01) at multivariate analysis (median OS for patients with or without rash: 42 wk vs 15 wk, respectively, Log-rank P = 0.03). Additional predictors of better outcome were: CA 19-9 reduction, female sex (for PFS), and good performance status (for OS). CONCLUSION: Primary study endpoint was not met. However, skin rash strongly predicted erlotinib efficacy, suggesting that a pharmacodynamic-based strategy for patient selection deserves further investigation.

[170]

TÍTULO / TITLE: - Comparison of Branch Duct and Main Pancreatic Duct Mural Nodules in Intraductal Papillary Mucinous Neoplasm.

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

REVISTA / JOURNAL: - Pancreas. 2013 Oct;42(7):1193-1195.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/MPA.0b013e31828f9725](#)

AUTORES / AUTHORS: - Tawada K; Ishihara T; Yamaguchi T; Tsuyuguchi T; Hara T; Tada M; Mikata R; Sakai Y; Sugiyama H; Saito M; Kurosawa J; Nishikawa T; Yoshitomi H; Ohtsuka M; Miyazaki M; Yokosuka O

INSTITUCIÓN / INSTITUTION: - Department of Medicine and Clinical Oncology, Graduate School of Medicine Chiba University Chiba, Japan dawadawa927@yahoo.co.jp
Department of Gastroenterology Chiba Cancer Center Chiba, Japan Department of Medicine and Clinical Oncology, Graduate School of Medicine Chiba University Chiba, Japan Department of Gastroenterology Chiba Cancer Center Chiba, Japan Department of Medicine and Clinical Oncology, Graduate School of Medicine Chiba University Chiba, Japan Department of General Surgery Graduate School of Medicine Chiba University Chiba, Japan Department of Medicine and Clinical Oncology, Graduate School of Medicine Chiba University Chiba, Japan.

[171]

TÍTULO / TITLE: - Chronic pancreatitis: A path to pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Lett. 2013 Aug 24. pii: S0304-3835(13)00590-9. doi: 10.1016/j.canlet.2013.08.015.

●● Enlace al texto completo (gratis o de pago) [1016/j.canlet.2013.08.015](#)

AUTORES / AUTHORS: - Pinho AV; Chantrill L; Rooman I

INSTITUCIÓN / INSTITUTION: - Cancer Research Program, The Kinghorn Cancer Centre, Garvan Institute of Medical Research, Sydney, Australia.

RESUMEN / SUMMARY: - Chronic pancreatitis predisposes to pancreatic cancer development and both diseases share a common etiology. A central role has been proposed for the digestive enzyme-secreting acinar cell that can undergo ductal metaplasia in the inflammatory environment of pancreatitis. This metaplastic change is now a recognised precursor of pancreatic cancer. Inflammatory molecules also foster tumour growth through autocrine and paracrine effects in the epithelium and the stroma. These insights have raised new opportunities such as the manipulation of inflammation as a preventive and/or therapeutic strategy for pancreatic cancer. Finally, we address the need for an in-depth study of the pancreatic acinar cells.

[172]

TÍTULO / TITLE: - Systemic Treatment of Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs): Current Approaches and Future Options.

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

REVISTA / JOURNAL: - Endocr Pract. 2013 Sep 6:1-30.

●● Enlace al texto completo (gratis o de pago) [4158/EP13262.RA](#)

AUTORES / AUTHORS: - Strosberg JR

INSTITUCIÓN / INSTITUTION: - H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida.

RESUMEN / SUMMARY: - Objective: To describe recent advances in treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs). Methods: A review of the published English language literature on therapy of GEP-NETs with a focus on practice-changing clinical trials. Results: Somatostatin analog treatment remains a cornerstone of GEP-NET therapy, primarily for patients with hormonally functional tumors and midgut carcinoids. The biologic agents everolimus and sunitinib have similar tumor-stabilizing effects in pancreatic NETs and are both approved for treatment of progressive low-intermediate grade tumors. Their role in non-pancreatic NETs remains controversial. Cytotoxic chemotherapy has significant activity in pancreatic NETs but modern prospective data is lacking. Radiolabeled somatostatin analogs will likely

become more widely available once phase III randomized studies are completed. Conclusions: New treatment options for GEP-NETs have become available, and highlight the necessity of developing predictive biomarkers which will allow for appropriate and individualized selection of therapy.

TÍTULO / TITLE: - MicroRNA-141, downregulated in pancreatic cancer, inhibited the cell proliferation and invasion by directly targeting MAP4K4.

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

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Sep 6.

●● Enlace al texto completo (gratis o de pago) [1158/1535-7163.MCT-13-](#)

[0296](#)

AUTORES / AUTHORS: - Zhao G; Wang B; Liu Y; Zhang JG; Deng SC; Qin Q; Tian K; Li X; Zhu S; Niu Y; Gong Q; Wang CY

INSTITUCIÓN / INSTITUTION: - 1Pancreatic Disease Institute, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology.

RESUMEN / SUMMARY: - Abstract MicroRNAs (miRNAs) are associated with various types of cancer due to their ability to affect expression of genes that modulate tumorigenesis. In this study, we explored the role of miR-141 in pancreatic cancer. The clinical characteristics analysis showed that miR-141 was significantly down-regulated in pancreatic cancer tissues and cell lines. Moreover, the decreased miR-141 was significantly associated with tumor size, TNM stage, lymph node and distant metastasis. Meanwhile, both Kaplan-Meier and multivariate survival analysis demonstrated decreased miR-141 were associated with overall survival. Overexpression of miR-141 in pancreatic cancer cells inhibited cell proliferation, clonogenicity and invasion, induced G1 arrest and apoptosis, and enhanced chemosensitivity. To understand how miR-141 mediates the phenotype of pancreatic cancer cells, a bioinformatics tool was used to identify MAP4K4 as a potential target of miR-141. The Dual-Luciferase reporter gene assay demonstrated that miR-141 binds directly to 3'UTR of MAP4K4 to inhibit MAP4K4 expression. Western blot and qRT-PCR analyses revealed that MAP4K4 expression was inversely correlated with miR-141 expression both in pancreatic cancer samples and cell lines. Knockdown of MAP4K4 inhibited cell proliferation, clonogenicity and invasion, induced G1 arrest and apoptosis, and enhanced chemosensitivity. In nude mice xenograft model, both overexpression of miR-141 and knockdown of MAP4K4 significantly repressed pancreatic cancer cell growth. Therefore, we conclude that miR-141 targets MAP4K4 and acts as a tumor suppressor in pancreatic cancer cells, and may serve as a novel therapeutic agent for miRNA-based pancreatic cancer therapy.

TÍTULO / TITLE: - Overcoming the stromal barrier for targeted delivery of HPMA copolymers to pancreatic tumors.

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

REVISTA / JOURNAL: - Int J Pharm. 2013 Nov 1;456(1):202-11. doi: 10.1016/j.ijpharm.2013.07.067. Epub 2013 Aug 8.

●● Enlace al texto completo (gratis o de pago) [1016/j.ijpharm.2013.07.067](#)

AUTORES / AUTHORS: - Buckway B; Wang Y; Ray A; Ghandehari H

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutics and Pharmaceutical Chemistry, and of Bioengineering, Utah Center for Nanomedicine, Nano Institute of Utah, University of Utah, 36 S Wasatch Dr, 5205 SMBB, Salt Lake City, UT 84112, USA; Center for Nanomedicine, Nano Institute of Utah, University of Utah, Salt Lake City, UT 84112, USA.

RESUMEN / SUMMARY: - Delivery of macromolecules to pancreatic cancer is inhibited by a dense extracellular matrix composed of hyaluronic acid, smooth muscle actin and collagen fibers. Hyaluronic acid causes a high intratumoral fluidic pressure which prevents diffusion and penetration into the pancreatic tumor. This study involves the breaking down of hyaluronic acid by treating CAPAN-1 xenograft tumors in athymic nu/nu mice with targeted N-(2-hydroxypropyl)methacrylamide (HPMA) copolymers radiolabeled with (111)In for single photon emission computerized tomography (SPECT) imaging. Two targeting strategies were investigated including alphavbeta3 integrin and HER2 receptors. HPMA copolymers were targeted to these receptors by conjugating short peptide ligands cRGDfK and KCCYSL to the side chains of the copolymer. Results demonstrate that tumor targeting can be achieved in vivo after treatment with hyaluronidase. This approach shows promise for enhanced delivery of polymer-peptide conjugates to solid tumors.

[174]

TÍTULO / TITLE: - Pancreatic tuberculosis presenting as an unusual head mass.

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

REVISTA / JOURNAL: - Endoscopy. 2013 Sep;45 Suppl 2:E317-8. doi: 10.1055/s-0033-1344565. Epub 2013 Sep 5.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1344565](#)

AUTORES / AUTHORS: - Rana SS; Chaudhary V; Gupta N; Sampath S; Mittal BR; Bhasin DK

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India.

[175]

TÍTULO / TITLE: - A rare cause of diarrhea: pancreatic VIPoma.

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

REVISTA / JOURNAL: - Endoscopy. 2013 Sep;45 Suppl 2:E311-2. doi: 10.1055/s-0033-1344411. Epub 2013 Sep 5.

●● Enlace al texto completo (gratuito o de pago) [1055/s-0033-1344411](#)

AUTORES / AUTHORS: - Johnson JB; Marsden L; Samadder NJ

INSTITUCIÓN / INSTITUTION: - Department of Medicine (Gastroenterology), Huntsman Cancer Institute and University of Utah, Salt Lake City, Utah, United States of America.

[176]

TÍTULO / TITLE: - A novel distinguishing system for the diagnosis of malignant pancreatic cystic neoplasm.

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

REVISTA / JOURNAL: - Eur J Radiol. 2013 Aug 8. pii: S0720-048X(13)00356-2. doi: 10.1016/j.ejrad.2013.06.028.

●● Enlace al texto completo (gratuito o de pago) [1016/j.ejrad.2013.06.028](#)

AUTORES / AUTHORS: - Shen X; Lu D; Xu X; Wang J; Wu J; Yan S; Zheng SS

INSTITUCIÓN / INSTITUTION: - Department of Radiology, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China. Electronic address: shanlixinc@163.com.

RESUMEN / SUMMARY: - PURPOSE: To explore a simple and reliable non-invasive distinguishing system for the pre-operative evaluation of malignancy in pancreatic cystic neoplasm (PCN). METHODS: This study first enrolled an observation cohort of 102 consecutive PCN patients. Demographic information, results of laboratory examinations, and computed tomography (CT) presentations were recorded and analyzed to achieve a distinguishing model/system for malignancy. A group of 21 patients was then included to validate the model/system prospectively. RESULTS: Based on the 11 malignancy-related features identified by univariate analysis, a distinguishing model for malignancy in PCN was established by multivariate analysis: PCN malignant score=2.967xelevated fasting blood glucose (FBG) (≥ 6.16 mmol/L)+/-4.496xasymmetrically thickened wall (or mural nodules ≥ 4 mm)+/-1.679xseptum thickening (≥ 2 mm)-5.134. With the optimal cut-off value selected as -2.8 in reference to the Youden index, the proposed system for malignant PCN was established: septum thickening (>2 mm), asymmetrically thickened wall (or mural nodules >4 mm), or elevated FBG (>6.16 mmol/L, accompanying commonly known malignant signs), the presence of at least one of these 3 features indicated malignancy in PCN. The accuracy, sensitivity and specificity of this system were 81.4%, 95.8% and 76.9%, respectively. MRI was performed on 32 patients, making correct prediction of malignancy explicitly in only 68.8% (22/32). The subsequent prospective validation study showed that the proposed distinguishing system had a predictive accuracy of 85.7% (18/21). Moreover, a higher model score, or aggregation of the features in the

proposed system, indicated a higher grade of malignancy (carcinoma) in PCN.
CONCLUSION: Elevated FBG (>6.16mmol/L), asymmetrically thickened wall (or mural nodules>4mm) and septum thickening (>2mm) are of great value in differentiating the malignancy in PCN. The developed distinguishing system is reliable in the diagnosis of malignant PCN.

[177]

TÍTULO / TITLE: - Phosphohistone h3 and ki-67 labeling indices in cytologic specimens from well-differentiated neuroendocrine tumors of the gastrointestinal tract and pancreas: a comparative analysis using automated image cytometry.

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

REVISTA / JOURNAL: - Acta Cytol. 2013;57(5):501-8. doi: 10.1159/000351475. Epub 2013 Sep 7.

●● Enlace al texto completo (gratis o de pago) [1159/000351475](#)

AUTORES / AUTHORS: - Fung AD; Cohen C; Kavuri S; Lawson D; Gao X; Reid MD

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Emory University School of Medicine, Atlanta, Ga., USA.

RESUMEN / SUMMARY: - Background: Ki-67 proliferation index was recently incorporated in the grading of neuroendocrine neoplasms (NENs) of the gastrointestinal tract (GIT) and pancreas. These are now divided into well-differentiated neuroendocrine tumors (WDNETs, grades 1 and 2) and poorly differentiated neuroendocrine carcinomas (grade 3). While Ki-67 is an established proliferation marker in NENs, phosphohistone H3 (PHH3), a newer marker of mitotic activity, is not. Methods: We determined Ki-67 and PHH3 indices on cytologic samples from WDNETs of the GIT and pancreas using an automated cellular imaging system (ACIS®). Results: There was a strong correlation between Ki-67 and PHH3 indices generated by ACIS on cytologic samples. However, in some cases the two stains caused conflicting grades within the same tumor. Conclusion: Both antibodies stain cells in different phases of the cell cycle which may cause discordant grades, thus affecting patient management and prognostication. Ki-67 staining is stronger than PHH3, making 'hot spots' easier to identify on ACIS. Ki-67 is more ideal than PHH3 for staining NENs, especially in tumors with borderline grades. Because PHH3 generates lower mitotic indices it should not be used as a proliferation marker in NENs until its expression has been further characterized. © 2013 S. Karger AG, Basel.

[178]

TÍTULO / TITLE: - Non-cirrhotic portal-systemic encephalopathy caused by enlargement of a splenorenal shunt after pancreaticoduodenectomy for locally advanced duodenal cancer: report of a case.

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

REVISTA / JOURNAL: - Surg Today. 2013 Aug 28.

●● Enlace al texto completo (gratis o de pago) [1007/s00595-013-0679-1](#)

AUTORES / AUTHORS: - Kasagi Y; Saeki H; Akahoshi T; Kawasaki J; Ando K; Oki E; Ohga T; Tomikawa M; Kakeji Y; Shirabe K; Maehara Y

INSTITUCIÓN / INSTITUTION: - Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, 812-8582, Japan, nanka_u_t@yahoo.co.jp.

RESUMEN / SUMMARY: - We report a case of portal-systemic encephalopathy occurring secondary to a splenorenal shunt, 2 years after a pancreaticoduodenectomy for locally advanced duodenal carcinoma. A 55-year-old woman was brought to our hospital with a decreased level of consciousness. Laboratory testing revealed an elevated serum ammonia level (221 µg/dl) and normal liver function. Retrospective review of a series of contrast-enhanced computed tomography scans of the abdomen identified a splenorenal shunt, which had gradually enlarged over the past 2 years (Fig. 1). The decreased level of consciousness was thought to be due to portal-systemic encephalopathy secondary to the splenorenal shunt. We performed balloon-occluded retrograde transvenous obliteration to occlude the splenorenal shunt, following which her serum ammonia level returned to normal (28 µg/dl) and an alert level of consciousness was maintained. Fig. 1 Review of abdominal computed tomography scans. a Preoperatively, b 6 months postoperatively, c 1 year postoperatively, d 2 years and 2 months postoperatively. The shunt vessel gradually enlarged after pancreaticoduodenectomy (circle).

[179]

TÍTULO / TITLE: - Endoscopic sonography and sonographically guided fine-needle aspiration biopsy in the diagnosis of unusual pancreatic metastases from synovial sarcoma.

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

REVISTA / JOURNAL: - J Clin Ultrasound. 2013 Sep 4. doi: 10.1002/jcu.22089.

●● Enlace al texto completo (gratis o de pago) [1002/jcu.22089](#)

AUTORES / AUTHORS: - Krishna SG; Rao BB; Lee JH

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Hepatology, and Nutrition, MD Anderson Cancer Center, Houston, TX, USA; Department of Gastroenterology, Hepatology, and Nutrition, Ohio State University Medical Center, Columbus, OH, USA.

RESUMEN / SUMMARY: - Pancreatic metastases are commonly solitary solid lesions frequently derived from primary renal cell carcinoma, lung cancer, or melanoma. Very few case reports have described cystic-appearing metastases in the pancreas and even fewer have reported a combination of cystic and solid metastatic lesions. Synovial

sarcoma is a rare and aggressive soft tissue neoplasm, frequently metastasizing to the lungs and bones. We present a case of primary synovial sarcoma with multiple solid and cystic-appearing pancreatic metastases diagnosed by endoscopic ultrasound and sonographically guided fine-needle aspiration. © 2013 Wiley Periodicals, Inc. J Clin Ultrasound, 2013.

[180]

TÍTULO / TITLE: - Number of examined lymph nodes and nodal status assessment in pancreaticoduodenectomy for pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Eur J Surg Oncol. 2013 Oct;39(10):1116-21. doi: 10.1016/j.ejso.2013.07.089. Epub 2013 Aug 12.

●● Enlace al texto completo (gratis o de pago) [1016/j.ejso.2013.07.089](#)

AUTORES / AUTHORS: - Vuarnesson H; Lupinacci RM; Semoun O; Svrcek M; Julie C; Balladur P; Penna C; Bachet JB; Resche-Rigon M; Paye F

INSTITUCIÓN / INSTITUTION: - Department of Digestive Surgery, UPMC University Pierre et Marie Curie, Paris VI, Hopital Saint Antoine, 184 rue du faubourg Saint Antoine, 75012 Paris, France.

RESUMEN / SUMMARY: - BACKGROUND: The accuracy of the assessment of the nodal status in resected cephalic pancreatic adenocarcinoma (PA) depends on the number of examined lymph nodes (NELN). This study assesses the impact of the NELN on N staging and survival and propose a minimal number of examined lymph nodes (MNELN) ensuring reliability of the pN status determination. METHODS: 188 consecutive patients treated by pancreaticoduodenectomy (PD) for PA. Correlations between NELN and survivals of pN0 and pN1 groups and with the rate of pN1 patients were studied. A probability model based on the binomial law was built to estimate the MNELN able to detect pN1 patients with a sensitivity $\geq 95\%$. RESULTS: Overall and disease free 5-year survivals were 27.2% and 24.6% respectively. 135 patients (71.8%) were staged pN1. The median NELN was 17 (range 0-68). Overall and disease free survivals of pN1 patients were not related to NELN. The influence of NELN on survival in pN0 patients due to stage migration did not reach significance. The probability model showed that a MNELN of 16 nodes was required to detect pN1 patients with a sensitivity of 95%. CONCLUSION: A MNELN of 16 is required to assess pN status and should be considered as a quality criterion in future studies and trials on PD for PA.

[181]

TÍTULO / TITLE: - Ectopic Duodenal Insulinoma: A Very Rare and Challenging Tumor Type. Description of a Case and Review of the Literature.

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

REVISTA / JOURNAL: - Endocr Pathol. 2013 Sep 5.

●● Enlace al texto completo (gratis o de pago) [1007/s12022-013-9262-y](https://doi.org/10.1007/s12022-013-9262-y)

AUTORES / AUTHORS: - La Rosa S; Pariani D; Marando A; Sessa F; Cortese F; Capella C

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RESUMEN / SUMMARY: - Although most insulinomas are located in the pancreas, very rare ectopic cases have been described in the spleen, perisplenic tissue, duodenohepatic ligament, and adjacent to the ligament of Treitz. Moreover, three cases located in the duodenum have also been reported in the English literature. Ectopic insulinomas represent challenging neoplasms with clinical implications mainly due to the difficulties in their pre-operative diagnosis and localization. In the present paper, we describe the fourth ectopic duodenal insulinoma so far reported. A 75-year-old woman presented at clinical observation due to neuroglycopenic symptoms that disappeared after glucose intake. Tumor was localized in the second portion of the duodenum in front of the papilla of Vater and was surgically enucleated. Microscopically, it was composed of monomorphic cells with eosinophilic cytoplasm arranged in trabecular and lobular patterns and diffusely positive for insulin, proinsulin, amylin, and PDX1. About 30 % of tumor cells also showed immunoreactivity for somatostatin, while no positivity for glucagon, pancreatic polypeptide, gastrin, serotonin, and somatostatin receptor subtype 2^a was found. The Ki67 proliferative index was 1 %. We have also reviewed the literature on this topic to give the reader a comprehensive overview of this very rare tumor type.

[182]

TÍTULO / TITLE: - Familial pancreatic cancer-status quo.

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

REVISTA / JOURNAL: - Int J Colorectal Dis. 2013 Aug 16.

●● Enlace al texto completo (gratis o de pago) [1007/s00384-013-1760-3](https://doi.org/10.1007/s00384-013-1760-3)

AUTORES / AUTHORS: - Fendrich V; Langer P; Bartsch DK

INSTITUCIÓN / INSTITUTION: - National Case Collection of Familial Pancreatic Cancer of the Deutsche Krebshilfe (FaPaCa), Department of Surgery, Philipps-University Marburg, Baldingerstrasse, 35043, Marburg, Germany, fendrich@med.uni-marburg.de.

RESUMEN / SUMMARY: - INTRODUCTION: Familial pancreatic cancer (FPC) is defined by families with at least two first-degree relatives with confirmed pancreatic ductal adenocarcinoma (PDAC) that do not fulfill the criteria of other inherited tumor syndromes with an increased risk for the development of PDAC, such as hereditary pancreatitis or hereditary breast and ovarian cancer. FPC is mostly autosomal dominant inherited and presents with a heterogeneous phenotype. Although the major gene defect has not yet been identified, some important germline mutations in the BRCA2-, PALB2-, and ATM-genes are causative in some FPC families. FPC

SCREENING: It is suggested by experts to include high-risk individuals in a screening program with a multidisciplinary approach under research protocol conditions. However, neither biomarkers nor reliable imaging modalities for the detection of high-grade precursor lesions are yet available. Most screening programs are currently based on endoscopic ultrasound and magnetic resonance imaging, and first data demonstrated that precursor lesions (pancreatic intraepithelial neoplasia, intraductal papillary mucinous neoplasm) of PDAC can be identified. Timing and extent of surgery are still a matter of debate. SCOPE OF THE REVIEW: The present review focuses on the clinical phenotype of FPC, its histopathological characteristics, known underlying genetic changes, genetic counseling, and screening.

[183]

TÍTULO / TITLE: - Efficacy of liposomal curcumin in a human pancreatic tumor xenograft model: inhibition of tumor growth and angiogenesis.

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

REVISTA / JOURNAL: - Anticancer Res. 2013 Sep;33(9):3603-9.

AUTORES / AUTHORS: - Ranjan AP; Mukerjee A; Helson L; Gupta R; Vishwanatha JK

INSTITUCIÓN / INSTITUTION: - Department of Molecular Biology and Immunology, and Institute for Cancer Research, Graduate School of Biomedical Sciences, University of North Texas Health Science Center, Fort Worth, Texas, 76107, USA.

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RESUMEN / SUMMARY: - BACKGROUND: Liposome-based drug delivery has been successful in the past decade, with some formulations being Food and Drug Administration (FDA)-approved and others in clinical trials around the world. The major disadvantage associated with curcumin, a potent anticancer agent, is its poor aqueous solubility and hence low systemic bioavailability. However, curcumin can be encapsulated into liposomes to improve systemic bioavailability. MATERIALS AND METHODS: We determined the antitumor effects of a liposomal curcumin formulation against human MiaPaCa pancreatic cancer cells both in vitro and in xenograft studies. Histological sections were isolated from murine xenografts and immunohistochemistry was performed. RESULTS: The in vitro (IC₅₀) liposomal curcumin proliferation-inhibiting concentration was 17.5 μM. In xenograft tumors in nude mice, liposomal curcumin at 20 mg/kg i.p. three-times a week for four weeks induced 42% suppression of tumor growth compared to untreated controls. A potent antiangiogenic effect characterized by a reduced number of blood vessels and reduced expression of vascular endothelial growth factor and annexin A2 proteins, as determined by immunohistochemistry was observed in treated tumors. CONCLUSION: These data clearly establish the efficacy of liposomal curcumin in reducing human pancreatic cancer growth in the examined model. The therapeutic curcumin-based effects, with

no limiting side-effects, suggest that liposomal curcumin may be beneficial in patients with pancreatic cancer.

[184]

TÍTULO / TITLE: - Comparison of pancreatic acinar cell carcinoma and adenocarcinoma using multidetector-row computed tomography.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Sep 14;19(34):5713-9. doi: 10.3748/wjg.v19.i34.5713.

●● Enlace al texto completo (gratis o de pago) [3748/wjg.v19.i34.5713](#)

AUTORES / AUTHORS: - Sumiyoshi T; Shima Y; Okabayashi T; Kozuki A; Nakamura T

INSTITUCIÓN / INSTITUTION: - Tatsuaki Sumiyoshi, Yasuo Shima, Takehiro Okabayashi, Akihito Kozuki, Toshio Nakamura, Departments of Gastroenterological Surgery, Kochi Health Sciences Center, Kochi 781-8555, Japan.

RESUMEN / SUMMARY: - AIM: To distinguish acinar cell carcinoma (ACC) from pancreatic adenocarcinoma (AC) by comparing their computed tomography findings. METHODS: Patients with ACC and AC were identified on the basis of results obtained using surgically resected pancreatotomy specimens. The preoperative computer tomographic images of 6 acinar cell carcinoma patients and 67 pancreatic adenocarcinoma patients in 4 phases (non-contrast, arterial, portal venous, and delayed phase) were compared. The scan delay times were 40, 70, and 120 s for each contrast-enhanced phase. The visual pattern, tomographic attenuation value, and time attenuation curve were assessed and compared between AC and ACC cases using the chi(2) test, Wilcoxon signed-rank test, and Mann Whitney U test. RESULTS: The adenocarcinomas tended to be hypodense in all 4 phases. The acinar cell carcinomas also tended to be hypodense in the 3 contrast-enhanced phases, although their computed tomographic attenuation values were higher. Further, 5 of the 6 acinar cell carcinomas (83%) were isodense in the non-contrast phase. The time attenuation curve of the adenocarcinomas showed a gradual increase through the 4 phases, and all adenocarcinomas showed peak enhancement during the delayed phase. The time attenuation curve of the acinar cell carcinomas showed peak enhancement during the portal venous phase in 4 cases and during the arterial phase in 2 cases. None of the 6 acinar cell carcinomas showed peak enhancement during the delayed phase. CONCLUSION: The tumor density in the non-contrast phase and time attenuation curve pattern clearly differ between acinar cell carcinomas and adenocarcinomas, and multidetector-row computed tomography can thus distinguish these tumors.

[185]

TÍTULO / TITLE: - Hepatitis B and pancreatic cancer.

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

REVISTA / JOURNAL: - Eur J Cancer Prev. 2013 Nov;22(6):620. doi: 10.1097/CEJ.0b013e32836034ac.

●● Enlace al texto completo (gratis o de pago) [1097/CEJ.0b013e32836034ac](#)

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[186]

TÍTULO / TITLE: - Laparoscopic splenic hilum lymph node dissection for advanced proximal gastric cancer: A modified approach for pancreas- and spleen-preserving total gastrectomy.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Aug 14;19(30):4992-9. doi: 10.3748/wjg.v19.i30.4992.

●● Enlace al texto completo (gratis o de pago) [3748/wjg.v19.i30.4992](#)

AUTORES / AUTHORS: - Mou TY; Hu YF; Yu J; Liu H; Wang YN; Li GX

INSTITUCIÓN / INSTITUTION: - Ting-Yu Mou, Yan-Feng Hu, Jiang Yu, Hao Liu, Ya-Nan Wang, Guo-Xin Li, Department of General Surgery, Nanfang Hospital, Southern Medical University, Guangzhou 510515, Guangdong Province, China.

RESUMEN / SUMMARY: - AIM: To investigate the feasibility and optimal approach for laparoscopic pancreas- and spleen-preserving splenic hilum lymph node dissection in advanced proximal gastric cancer. METHODS: Between August 2009 and August 2012, 12 patients with advanced proximal gastric cancer treated in Nanfang Hospital, Southern Medical University, Guangzhou, China were enrolled and subsequently underwent laparoscopic total gastrectomy with pancreas- and spleen-preserving splenic hilum lymph node (LN) dissection. The clinicopathological characteristics, surgical outcomes, postoperative course and follow-up data of these patients were retrospectively collected and analyzed in the study. RESULTS: Based on our anatomical understanding of peripancreatic structures, we combined the characteristics of laparoscopic surgery and developed a modified approach (combined supra- and infra-pancreatic approaches) for laparoscopic pancreas- and spleen-preserving splenic hilum LN dissection. Surgery was completed in all 12 patients laparoscopically without conversion. Only one patient experienced intraoperative bleeding when dissecting LNs along the splenic artery and was handled with laparoscopic hemostasis. The mean operating time was 268.4 min and mean number of retrieved splenic hilum LNs was 4.8. One patient had splenic hilum LN metastasis (8.3%). Neither postoperative

morbidity nor mortality was observed. Peritoneal metastasis occurred in one patient and none of the other patients died or experienced recurrent disease during the follow-up period. CONCLUSION: Laparoscopic total gastrectomy with pancreas- and spleen-preserving splenic hilum LN dissection using the modified approach for advanced proximal gastric cancer could be safely achieved.

[187]

TÍTULO / TITLE: - Pancreatectomy Versus Conservative Management for Pancreatic Cancer: A Question of Lead-time Bias.

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

REVISTA / JOURNAL: - Am J Clin Oncol. 2013 Sep 21.

●● Enlace al texto completo (gratis o de pago) [1097/COC.0b013e3182a533ea](https://doi.org/10.1097/COC.0b013e3182a533ea)

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INSTITUCIÓN / INSTITUTION: - *Division of Radiation Oncology, University of Ottawa
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RESUMEN / SUMMARY: - OBJECTIVES:: Pancreatectomy is regarded as the only curative treatment for cancer of the pancreas. A population-based study was conducted to examine its efficacy within the general community. METHODS:: Overall and cancer-specific survivals were compared between individuals treated with pancreatectomy and those managed nonsurgically. Kaplan-Meier analysis was used, based on both time from diagnosis and attained age (age at diagnosis plus time from diagnosis). RESULTS:: A total of 7830 Surveillance Epidemiology and End Results cases of localized cancer of the pancreatic head were retrieved, diagnosed from 2000 to 2008. Median follow-up was 12 months; the pancreatectomy cohort was 5 years younger and had 7-fold less stage III disease. Overall and cancer-specific survivals were 17% and 21% at 5 years from time of diagnosis in the pancreatectomy cohort versus 2% and 4% in the nonsurgical cohort, respectively (P<0.001). However, the overall and cancer-specific survival curves were nearly superimposed on each other when based on attained age. Moreover, the proportion of deaths attributable to pancreatic cancer exceeded 85% in both cohorts. CONCLUSIONS:: A lead-time bias is hypothesized to explain the survival discrepancies seen between time from diagnosis and attained age analyses; the pancreatectomy cohort was diagnosed earlier, with less disease. If most of these individuals had occult metastases at diagnosis, which manifested later and caused death at similar ages as the nonsurgical cohort, their survival from time of diagnosis would appear speciously improved. A randomized controlled trial would be necessary to confirm whether or not the survival advantage ascribed to pancreatectomy should be attributed to lead-time bias.

[188]

TÍTULO / TITLE: - CD40 EXPRESSION IN PANCREATIC CANCER.

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

REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Sep 20. doi: 10.5754/hge13421.

●● Enlace al texto completo (gratis o de pago) [5754/hge13421](#)

AUTORES / AUTHORS: - Unek T; Unek IT; Agalar AA; Sagol O; Ellidokuz H; Ertener O; Oztop I; Karademir S; Yilmaz U; Astarcioglu I

RESUMEN / SUMMARY: - Background: CD40, a tumor necrosis factor receptor family member, is expressed in a variety of cell types. This widespread expression suggests that CD40 may play an important role in normal physiology and disease pathogenesis. The objective of the current study was to investigate the expression of CD40, and its association with clinicopathological features and survival in patients with pancreatic ductal adenocarcinoma. Methodology: CD40 expression was assessed in 53 pancreatic ductal adenocarcinoma surgical specimens by immunohistochemistry, and expression was correlated with patient clinicopathological parameters and outcome. Results: Among 53 pancreatic cancer specimens, CD40 expression was detected in 13 specimens (24.5%), and peritumoral lymphocytes were present in 45 specimens (84.9%). Patients with CD40-positive tumors exhibited prolonged median disease-free survival (DFS) compared with patients with CD40-negative tumors (15.60+/-3.87 versus 10.03+/-1.92); however, this was not significant (p=0.845). Patients with peritumoral lymphocytic reaction exhibited prolonged median DFS compared with patients without peritumoral lymphocytes (10.96+/-1.40 versus 7.60+/-0.47); however, this was not significant (p=0.624). Patients with peritumoral lymphocytic reaction exhibited higher median overall survival compared with patients without peritumoral lymphocytes (15.20+/-1.78 versus 10.13+/-1.39); however, again this was not significant (p=0.100). Conclusions: These results suggest that CD40 expression on pancreatic cancer cells and peritumoral lymphocytic reaction may serve as prognostic markers.

[189]

TÍTULO / TITLE: - Discovery of novel candidate oncogenes in pancreatic carcinoma using high-throughput microarrays.

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

REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Sep 12. doi: 10.5754/hge13343.

●● Enlace al texto completo (gratis o de pago) [5754/hge13343](#)

AUTORES / AUTHORS: - Jiang Y; Liu M; Li Z; Jiang Y

RESUMEN / SUMMARY: - Pancreatic cancer is one of the most aggressive tumors in mankind. Its aggressiveness is only due to the biological progressive characteristics but also the difficulty for clinical early detection which urges us to find diagnostic tools to help make an early diagnosis. Molecular medicine studying bio-markers is one developing tool by measuring the molecules such as proteins, DNAs or RNAs in the

blood sample or suspected tumor tissue. The molecular dysregulation is believed to play major roles in tumorigenesis or a result after the tumor formation and can be used as a bio-marker for tumor detection. In this paper, we studied the gene expression profiles using tissues from pancreatic cancer patients. We observed dysregulation of gene expression profiles using high-throughput sequencing technique and verified three gene upregulation, REG4, CDH3 and S100P both in pancreatic cell lines and carcinoma tissues by RT-PCR and Northern Blot. A detailed description of the genes involved is listed within this article. We believe by unraveling the gene dysregulation profiles in pancreatic tumor tissues can we achieve an early and precise diagnosis of pancreatic cancer. Moreover, these newly found genes, due to their functions involved in cell migration and mitosis, may play major roles in tumorigenesis.

[190]

TÍTULO / TITLE: - Retroperitoneal cavernous hemangioma resected by a pylorus preserving pancreaticoduodenectomy.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Jul 28;19(28):4624-9. doi: 10.3748/wjg.v19.i28.4624.

●● [Enlace al texto completo \(gratis o de pago\) 3748/wjg.v19.i28.4624](#)

AUTORES / AUTHORS: - Hanaoka M; Hashimoto M; Sasaki K; Matsuda M; Fujii T; Ohashi K; Watanabe G

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RESUMEN / SUMMARY: - A retroperitoneal hemangioma is a rare disease. We report on the diagnosis and treatment of a retroperitoneal hemangioma which had uncommonly invaded into both the pancreas and duodenum, thus requiring a pylorus preserving pancreaticoduodenectomy (PpPD). A 36-year-old man presented to our hospital with abdominal pain. An enhanced computed tomography scan without contrast enhancement revealed a 12 cm x 9 cm mass between the pancreas head and right kidney. Given the high rate of malignancy associated with retroperitoneal tumors, surgical resection was performed. Intraoperatively, the tumor was inseparable from both the duodenum and pancreas and PpPD was performed due to the invasive behavior. Although malignancy was suspected, pathological diagnosis identified the tumor as a retroperitoneal cavernous hemangioma for which surgical resection was the proper diagnostic and therapeutic procedure. Retroperitoneal cavernous hemangioma is unique in that it is typically separated from the surrounding organs. However, clinicians need to be aware of the possibility of a case, such as this, which has invaded into the surrounding organs despite its benign etiology. From this case, we recommend that combined resection of inseparable organs should be performed if the mass has invaded into other tissues due to the hazardous nature of local

recurrence. In summary, this report is the first to describe a case of retroperitoneal hemangioma that had uniquely invaded into surrounding organs and was treated with PpPD.

[191]

TÍTULO / TITLE: - Preclinical evaluation of herpes simplex virus armed with granulocyte-macrophage colony-stimulating factor in pancreatic carcinoma.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Aug 21;19(31):5138-43. doi: 10.3748/wjg.v19.i31.5138.

●● [Enlace al texto completo \(gratis o de pago\) 3748/wjg.v19.i31.5138](#)

AUTORES / AUTHORS: - Liu H; Yuan SJ; Chen YT; Xie YB; Cui L; Yang WZ; Yang DX; Tian YT

INSTITUCIÓN / INSTITUTION: - Hao Liu, Ying-Tai Chen, Yi-Bin Xie, Liang-Cui, Yan-Tao Tian, Department of Abdominal Surgery, Cancer Hospital, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing 100021, China.

RESUMEN / SUMMARY: - AIM: To investigate the therapeutic efficacy and mechanisms of action of oncolytic-herpes-simplex-virus encoding granulocyte-macrophage colony-stimulating factor (HSV(GM-CSF)) in pancreatic carcinoma. METHODS: Tumor blocks were homogenized in a sterile grinder in saline. The homogenate was injected into the right armpit of each mouse. After vaccination, the mice were randomly assigned into four groups: a control group, a high dose HSV(GM-CSF) group [1×10^7 plaque forming units (pfu)/tumor], a medium dose HSV(GM-CSF) group (5×10^6 pfu/tumor) and a low dose HSV(GM-CSF) group (5×10^5 pfu/tumor). After initiation of drug administration, body weights and tumor diameters were measured every 3 d. Fifteen days later, after decapitation of the animal by cervical dislocation, each tumor was isolated, weighed and stored in 10% formaldehyde solution. The drug effectiveness was evaluated according to the weight, volume and relative volume change of each tumor. Furthermore, GM-CSF protein levels in serum were assayed by enzyme-linked immunosorbent assays at 1, 2, 3 and 4 d after injection of HSV(GM-CSF). RESULTS: Injection of the recombinant mouse HSV encoding GM-CSF resulted in a significant reduction in tumor growth compared to the control group, and dose-dependent effects were observed: the relative tumor proliferation rates of the low dose, medium dose and high dose groups on 15 d after injection were 45.5%, 55.2% and 65.5%, respectively. The inhibition rates of the tumor weights of the low, middle, and high dose groups were 41.4%, 46.7% and 50.5%, respectively. Furthermore, the production of GM-CSF was significantly increased in the mice infected with HSV(GM-CSF). The increase in the GM-CSF level was more pronounced in the high dose group compared to the other two dose groups. CONCLUSION: Our study provides the first evidence that HSV(GM-CSF) could inhibit the growth of pancreatic cancer. The enhanced GM-CSF expression might be responsible for the phenomenon.

[192]

TÍTULO / TITLE: - Bile duct carcinoma involving the common channel associated with pancreaticobiliary maljunction shows an extension pattern similar to ductal carcinoma of the pancreas.

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

REVISTA / JOURNAL: - Pathol Int. 2013 Aug;63(8):415-8. doi: 10.1111/pin.12085.

●● Enlace al texto completo (gratis o de pago) [1111/pin.12085](#)

AUTORES / AUTHORS: - Yoshida N; Esaki M; Kishi Y; Shimada K; Ojima H; Kanai Y; Hiraoka N

INSTITUCIÓN / INSTITUTION: - Division of Molecular Pathology, National Cancer Center Research Institute, Tokyo, Japan; Hepato-Biliary and Pancreatic Surgery Division, National Cancer Center Hospital, Tokyo, Japan.

RESUMEN / SUMMARY: - Biliary tract cancer occurs frequently in patients with pancreaticobiliary maljunction (PBM), although no details of its clinicopathological characteristics have been reported. Here we describe a case of bile duct (BD) cancer that developed in association with PBM. This BD cancer involved the common channel, extended to the main pancreatic duct (MPD) via the common channel, and invaded the pancreatic parenchyma, where its growth and spread, and features of its recurrence, were similar to those of ductal carcinoma of the pancreas. We assumed that MPD extension of BD cancer via the common channel was the reason for its deep spread to the pancreas, since BD cancer usually spreads along the BD and rarely reaches the common channel of the ampulla of Vater. During the follow-up of patients with PBM, attention should be paid to involvement of the common channel by BD cancer and also to cancer developing silently in the pancreas after extrahepatic BD resection.

[193]

TÍTULO / TITLE: - Comparison of Two Syngeneic Orthotopic Murine Models of Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - J Invest Surg. 2013 Aug 19.

●● Enlace al texto completo (gratis o de pago) [3109/08941939.2013.797057](#)

AUTORES / AUTHORS: - Nikfarjam M; Yeo D; He H; Baldwin G; Fifis T; Costa P; Tan B; Yang E; Wen SW; Christophi C

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Austin Health, University of Melbourne, Austin Health, LTB8, Heidelberg, Victoria, Australia.

RESUMEN / SUMMARY: - ABSTRACT Background: Pancreatic adenocarcinoma has an extremely poor prognosis. The use of appropriate in vivo models is essential in devising methods to improve treatment outcomes. Methods: A pancreatic adenocarcinoma

model based on tumor injection into the pancreatic head was compared with a pancreatic tail injection model in C57/BL6 mice. The murine pancreatic adenocarcinoma cell line PAN02, dispersed in Matrigel™, was used for tumor induction. Results: Tumors developed in all animals in both models. Tumor size was more consistent within the pancreatic tail group at 20 days following induction, with no evidence of metastatic disease. Animals in the pancreatic head injection group showed signs of reduced health by 20 days following injection and developed jaundice. Microscopic liver metastases were noted in some of these animals at this time point. The overall survival of animals at 40 days following tumor induction was significantly lower in the pancreatic head injection group (0% vs. 35%; $p < .001$). Multiple liver metastases were noted in five of 10 (50%) animals in the head injection group, without evidence of peritoneal metastases. In the pancreatic tail injection group, 18 of 20 (90%) animals had multiple peritoneal metastases, and nine of 20 (45%) animals had evidence of isolated liver deposits. Tumors in both regions of the pancreas had similar histologic characteristics, with a dense fibrotic stroma at the interface between the tumor and the normal pancreas. Conclusion: Pancreatic head and tail orthotopic cancer models produce consistent tumors, but the patterns of tumor spread and survival differ according to the site of injection.

[194]

TÍTULO / TITLE: - Pancreatic cancer in the remnant pancreas following primary pancreatic resection.

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

REVISTA / JOURNAL: - Surg Today. 2013 Aug 22.

●● Enlace al texto completo (gratis o de pago) [1007/s00595-013-0708-0](https://doi.org/10.1007/s00595-013-0708-0)

AUTORES / AUTHORS: - Hashimoto D; Chikamoto A; Ohmuraya M; Sakata K; Miyake K; Kuroki H; Watanabe M; Beppu T; Hirota M; Baba H

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery, Kumamoto University Graduate School of Medical Sciences, 1-1-1 Honjo, Kumamoto, 860-8556, Japan.

RESUMEN / SUMMARY: - PURPOSE: To clarify the clinical features of cancer in the pancreatic remnant. METHODS: We retrospectively reviewed the clinical and pathological findings of 10 patients who developed remnant pancreatic cancer in our hospital between 2002 and 2012. The KRAS sequences in both the initial pancreatic tumor and remnant pancreatic cancer were examined in two patients. RESULTS: Eight patients underwent a second pancreatectomy for remnant pancreatic cancer (resected group), while two patients were not operated on and underwent chemotherapy (unresected group). The remnant pancreatic cancer developed at the cut end of the pancreas (pancreaticogastrostomy site) in four patients. In the resected group, four patients died 17 months after the emergence of the remnant pancreatic cancer and

four patients survived during the median 40.5-month observation period. The median survival of the unresected group after the emergence of the remnant pancreatic cancer was 10 months. The findings of the KRAS sequencing and immunohistological staining of the remnant pancreatic cancer for MUC1 and MUC2 in the two patients were consistent with those of the initial pancreatic tumor in one patient, and not consistent in the other. CONCLUSIONS: Our results suggest that both local recurrence and a new primary cancer can develop in the pancreatic remnant, and repeated pancreatectomy can prolong survival.

[195]

TÍTULO / TITLE: - Cleistanthane diterpenes from the seed of *Caesalpinia sappan* and their antiausterity activity against PANC-1 human pancreatic cancer cell line.

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

REVISTA / JOURNAL: - *Fitoterapia*. 2013 Aug 31;91C:148-153. doi: 10.1016/j.fitote.2013.08.018.

●● Enlace al texto completo (gratis o de pago) [1016/j.fitote.2013.08.018](https://doi.org/10.1016/j.fitote.2013.08.018)

AUTORES / AUTHORS: - Nguyen HX; Nguyen MT; Nguyen TA; Nguyen NY; Phan DA; Thi PH; Nguyen TH; Dang PH; Nguyen NT; Ueda JY; Awale S

INSTITUCIÓN / INSTITUTION: - Faculty of Chemistry, University of Science, Vietnam National University-Ho Chi Minh City, Viet Nam.

RESUMEN / SUMMARY: - Three new cleistanthane diterpenes named tomocinon (1), tomocinol A (2), and tomocinol B (3), were isolated from the EtOAc extract of the seed of *Caesalpinia sappan*. Their structures were determined by extensive NMR spectroscopic analysis. The absolute stereochemistry of tomocinon (1) has been established by CD spectroscopic analysis. Cleistanthane diterpenes (1-3) represents the novel class of antiausterity agents having preferential cytotoxicity against PANC-1 human pancreatic cancer cell line under nutrient deprived condition with PC50 value of 34.7µM, 42.4µM and 39.4µM, respectively.

[196]

TÍTULO / TITLE: - Single-access laparoscopic subtotal spleno-pancreatectomy for pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - *Minim Invasive Ther Allied Technol*. 2013 Sep 18.

●● Enlace al texto completo (gratis o de pago) [3109/13645706.2013.841253](https://doi.org/10.1007/s13645706.2013.841253)

AUTORES / AUTHORS: - Bracale U; Lazzara F; Andreuccetti J; Stabilini C; Pignata G

INSTITUCIÓN / INSTITUTION: - General and Mini-Invasive Surgery, "San Camillo" Hospital, Trento, Italy.

RESUMEN / SUMMARY: - Abstract Laparoscopic distal or subtotal pancreatectomy can be performed safely and effectively unless there is a clear reason why not to do so. With the aim of reducing postoperative trauma and improving the cosmesis, single-access laparoscopic surgery has been introduced into daily practice. We report the first case of distal single-access laparoscopic pancreatectomy for an adenocarcinoma. The procedure was carried out in 170 minutes without postoperative complications. Despite some technical difficulties, we think that a single-access laparoscopic approach could be adequate for a pancreatic resection. However, an adequate analysis of cost-effectiveness as well as regarding the reproducibility should be carried out.

[197]

TÍTULO / TITLE: - Triptolide induces apoptosis and inhibits the growth and angiogenesis of human pancreatic cancer cells by downregulating COX-2 and VEGF.

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

REVISTA / JOURNAL: - Oncol Res. 2013;20(8):359-68. doi: 10.3727/096504013X13657689382932.

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

[3727/096504013X13657689382932](#)

AUTORES / AUTHORS: - Ma JX; Sun YL; Wang YQ; Wu HY; Jin J; Yu XF

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Fudan University, Shanghai, China.

RESUMEN / SUMMARY: - Triptolide (TPL) inhibits the growth and proliferation of a wide range of human cancer cells, but the underlying mechanism is largely unknown. Here, we report that TPL induces apoptosis and inhibits proliferation of PANC-1 pancreatic cancer cells by downregulating cyclooxygenase-2 (COX-2) and vascular endothelial growth factor (VEGF). Cell viability and apoptosis were measured by MTT assay and flow cytometry. Real-time PCR and Western blot were used to examine the expression of COX-2 and VEGF. The Matrigel angiogenesis and Transwell migration were employed to assess tube formation and cell migration. Pancreatic cancer mouse xenografts were established to investigate the in vivo antitumor effects of TPL. TUNEL staining and immunohistochemistry were used to detect the apoptosis rate and protein expression in tumor tissues. TPL inhibited the proliferation of pancreatic cancer cells in a time and concentration-dependent manner and decreased the expression of COX-2 and VEGF in vitro. Furthermore, medium from TPL-treated PANC-1 cells inhibited the proliferation, migration, and tube formation of HUVECs. TPL significantly reduced the growth of pancreatic cancer mouse xenografts, accompanied by an induction of apoptosis, inhibition of angiogenesis, and reduction of COX-2 and VEGF. Our data indicate that suppressing the expression of COX-2 and VEGF may be one of the molecular mechanisms by which TPL induces apoptosis and inhibits the growth and angiogenesis of human pancreatic cancer cells.

[198]

TÍTULO / TITLE: - Outcome and toxicity of salvage therapy with Lu-octreotate in patients with metastatic gastroenteropancreatic neuroendocrine tumours.

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

REVISTA / JOURNAL: - Eur J Nucl Med Mol Imaging. 2013 Sep 13.

●● Enlace al texto completo (gratis o de pago) [1007/s00259-013-2547-z](#)

AUTORES / AUTHORS: - Sabet A; Haslerud T; Pape UF; Sabet A; Ahmadzadehfar H; Grunwald F; Gohlke S; Biersack HJ; Ezziddin S

INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, University Hospital Bonn, Sigmund-Freud-Str. 25, 53105, Bonn, Germany.

RESUMEN / SUMMARY: - **PURPOSE:** We assessed the outcome and toxicity of salvage therapy (repeat treatment) with ¹⁷⁷Lu-octreotate and high cumulative activities in patients with metastatic gastroenteropancreatic neuroendocrine tumours (GEP-NET). **METHODS:** We retrospectively analysed a consecutive cohort of 33 patients with metastatic GEP-NET who underwent salvage peptide receptor radionuclide therapy (PRRT) in our institution. All patients had progressive NET prior to salvage treatment and had shown an initial response to PRRT. The mean cumulative activity was 44.3 GBq (30.0-83.7 GBq). Radiographic response was assessed using CT and/or MRI according to modified SWOG criteria. Toxicity was evaluated using laboratory data, including complete blood counts and renal function tests using CTCAE 3.0. Survival analysis was performed with the Kaplan-Meier curve method and a significance level at $p < 0.05$. **RESULTS:** Radiographic responses consisted of complete response in 1 patient (3.0 %), partial response in 6 patients (18.2 %), minor response in 1 patient (3.0 %), stable disease in 14 patients (42.4 %), and progressive disease in 11 patients (33.3 %). Median progression-free survival (PFS) from the start of salvage therapy was 13 months (95 % CI 9-18) and patients with a history of a durable PFS after initial PRRT tended to have long-lasting PFS after salvage treatment ($p = 0.04$). None of the patients developed severe nephrotoxicity (grade ≥ 3) or a myelodysplastic syndrome during follow-up. Relevant albeit reversible haematotoxicity (grade ≥ 3) occurred in 7 patients (21.2 %). The cumulative administered activity was not associated with an increased incidence of haematotoxicity. **CONCLUSION:** PRRT with ¹⁷⁷Lu-octreotate in the re-treatment setting is safe and effective in patients with metastatic GEP-NET.

[199]

TÍTULO / TITLE: - Phase II Study of Dasatinib (BMS-354825) in Patients With Metastatic Adenocarcinoma of the Pancreas.

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

REVISTA / JOURNAL: - Oncologist. 2013 Sep 26.

●● Enlace al texto completo (gratis o de pago) [1634/theoncologist.2013-](https://doi.org/10.1038/1634_theoncologist.2013-0255)

[0255](https://doi.org/10.1038/1634_theoncologist.2013-0255)

AUTORES / AUTHORS: - Chee CE; Krishnamurthi S; Nock CJ; Meropol NJ; Gibbons J; Fu P; Bokar J; Teston L; O'Brien T; Gudena V; Reese A; Bergman M; Saltzman J; Wright JJ; Dowlati A; Brell J

INSTITUCIÓN / INSTITUTION: - University Hospitals Seidman Cancer Center and.

RESUMEN / SUMMARY: - **BACKGROUND:** Src, EphA2, and platelet-derived growth factor receptors alpha and beta are dysregulated in pancreatic ductal adenocarcinoma (PDAC). Dasatinib is an oral multitarget tyrosine kinase inhibitor that targets BCR-ABL, c-Src, c-KIT, platelet-derived growth factor receptor beta, and EphA2. We conducted a phase II, single-arm study of dasatinib as first-line therapy in patients with metastatic PDAC. **METHODS:** Dasatinib (100 mg twice a day, later reduced to 70 mg twice a day because of toxicities) was orally administered continuously on a 28-day cycle. The primary endpoint was overall survival (OS). Response was measured using the Response Evaluation Criteria in Solid Tumors. Circulating tumor cells (CTCs) were also collected. **RESULTS:** Fifty-one patients enrolled in this study. The median OS was 4.7 months (95% confidence interval [CI]: 2.8-6.9 months). Median progression-free survival was 2.1 months (95% CI: 1.6-3.2 months). In 34 evaluable patients, the best response achieved was stable disease in 10 patients (29.4%). One patient had stable disease while on treatment for 20 months. The most common nonhematologic toxicities were fatigue and nausea. Edema and pleural effusions occurred in 29% and 6% of patients, respectively. The number of CTCs did not correlate with survival. **CONCLUSION:** Single-agent dasatinib does not have clinical activity in metastatic PDAC.

[200]

TÍTULO / TITLE: - Influence of MRE11, RAD50 and NIBRIN protein expression on survival in pancreatic carcinoma after curative resection.

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

REVISTA / JOURNAL: - Pathol Res Pract. 2013 Jul 26. pii: S0344-0338(13)00186-6. doi: 10.1016/j.prp.2013.07.003.

●● Enlace al texto completo (gratis o de pago) [1016/j.prp.2013.07.003](https://doi.org/10.1016/j.prp.2013.07.003)

AUTORES / AUTHORS: - Horst K; Ganzera S; Kaisers W; Munding J; Flott-Rahmel B; Tannapfel A; Zirngibl H

INSTITUCIÓN / INSTITUTION: - Department of Orthopedic Trauma Surgery, RWTH Aachen, Aachen, Germany. Electronic address: khorst@ukaachen.de.

RESUMEN / SUMMARY: - The MRE11/RAD50/NIBRIN complex, a protein complex that repairs DNA double-strand breaks, could serve as an early marker for new lesions in pancreatic cancer. We determined the expression of MRE11, RAD50 and NIBRIN, and their possible prognostic value regarding survival. Forty-one patients with ductal adenocarcinoma of the pancreas were included. All underwent curative surgery.

Immunohistochemistry was performed for MRE11, RAD50 and NIBRIN. Subsequent analyses were based on a modified immunoreactive score. Statistical analysis was conducted using the statistics program "R". The mean follow-up period was 509 days. The mean age of the patients was 67+/-8 years, male=56%, female=44%. Eighty-seven percent underwent a Kausch-Whipple procedure, whereas a left side resection was performed in 22% of patients. Positive lymph nodes were found in 80% of cases, and patients were staged UICC IIa (12%), IIb (56%) and IV (29%). Overall significant results were found for MRE11 (p=0.02) and NIBRIN (p=0.01) expression and postoperative survival. We found a significant relation between the expression of MRE11, NIBRIN and the postoperative survival of patients with ductal adenocarcinoma. The link between the expression of the MRN complex, ATM and pancreatic cancer can be used to develop new treatment options for pancreatic carcinoma.

[201]

TÍTULO / TITLE: - The controversial role of chemoradiation for patients with locally advanced pancreatic cancer.

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

REVISTA / JOURNAL: - Oncologist. 2013;18(9):981-5. doi: 10.1634/theoncologist.2013-0270. Epub 2013 Sep 10.

●● Enlace al texto completo (gratis o de pago) [1634/theoncologist.2013-](#)

[0270](#)

AUTORES / AUTHORS: - Faris JE; Wo JY

INSTITUCIÓN / INSTITUTION: - Massachusetts General Hospital Cancer Center, Harvard Medical School.

[202]

TÍTULO / TITLE: - Phase II Trial of Erlotinib Plus Gemcitabine Chemotherapy in Korean Patients with Advanced Pancreatic Cancer and Prognostic Factors for Chemotherapeutic Response.

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

REVISTA / JOURNAL: - Gut Liver. 2013 Sep;7(5):611-5. doi: 10.5009/gnl.2013.7.5.611. Epub 2013 Jun 11.

●● Enlace al texto completo (gratis o de pago) [5009/gnl.2013.7.5.611](#)

AUTORES / AUTHORS: - Park S; Chung MJ; Park JY; Chung JB; Bang S; Park SW; Song SY

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Graduate School, Yonsei University College of Medicine, Seoul, Korea. ; Center for Health Promotion, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - BACKGROUND/AIMS: Erlotinib and gemcitabine combined chemotherapy is becoming the treatment of choice in advanced pancreatic cancer.

We evaluated the effectiveness of treatment with erlotinib plus gemcitabine and the prognostic factors for chemotherapeutic response in Korean pancreatic cancer patients. METHODS: Sixty-nine patients with advanced pancreatic cancer who were treated with daily erlotinib 100 mg orally and gemcitabine 1,000 mg/m²/30 min intravenous infusion on days 1, 8, and 15 of each 4-week cycle from 2006 to 2009 were included in this study. This study was a phase II single-center trial. RESULTS: All 69 patients with advanced pancreatic cancer were chemotherapy-naive. The objective response rate was 18.8%, and the overall tumor-stabilization rate was 49.2%. The median overall survival was 7.7 months (95% confidence interval [CI], 6.0 to 9.4 months). The median progression-free survival was 1.9 months (95% CI, 1.4 to 2.5 months). Prognostic factors for good chemotherapeutic response were good performance status and the presence of skin rash during chemotherapy. Patients with lower performance scores showed worse chemotherapeutic responses (odds ratio [OR], 7.6; 95% CI, 2.4 to 24.8). Poor responses were predicted by the absence of skin rash during chemotherapy (OR, 3.0; 95% CI, 1.4 to 6.3). CONCLUSIONS: Erlotinib and gemcitabine chemotherapy is a tolerable treatment regimen and has a favorable therapeutic effect in Korean patients with advanced pancreatic cancer.

[203]

TÍTULO / TITLE: - Phase I study evaluating the treatment of patients with locally advanced pancreatic cancer with carbon ion radiotherapy: the PHOENIX-01 trial.

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

REVISTA / JOURNAL: - BMC Cancer. 2013 Sep 14;13(1):419.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-419](#)

AUTORES / AUTHORS: - Combs SE; Habermehl D; Kieser M; Dreher C; Werner J; Haselmann R; Jakel O; Jager D; Buchler MW; Debus J

RESUMEN / SUMMARY: - BACKGROUND: Treatment options for patients with locally advanced pancreatic cancer include surgery, chemotherapy as well as radiotherapy. In many cases, surgical resection is not possible, and therefore treatment alternatives have to be performed. Chemoradiation has been established as a convincing treatment alternative for locally advanced pancreatic cancer. Carbon ions offer physical and biological characteristics. Due to their inverted dose profile and the high local dose deposition within the Bragg peak precise dose application and sparing of normal tissue is possible. Moreover, in comparison to photons, carbon ions offer an increased relative biological effectiveness (RBE), which can be calculated between 1.16 and 2.46 depending on the pancreatic cancer cell line as well as the endpoint analyzed. Japanese Data on the evaluation of carbon ion radiation therapy showed promising results for patients with pancreatic cancer. Methods and design: The present PHOENIX-01 trial evaluates carbon ion radiotherapy using the active rasterscanning technique in patients with advanced pancreatic cancer in combination with weekly gemcitabine and adjuvant gemcitabine. Primary endpoint is toxicity, secondary

endpoints are overall survival, progression-free survival and response. DISCUSSION: The physical and biological properties of the carbon ion beam promise to improve the therapeutic ratio in patients with pancreatic cancer: Due to the inverted dose profile dose deposition in the entry channel of the beam leads to sparing of normal tissue; the Bragg peak can be directed into the defined target volume, and the sharp dose fall-off thereafter again spares normal tissue behind the target volume. The higher RBE of carbon ions, which has been shown also for pancreatic cancer cell lines in the preclinical setting, is likely to contribute to an increase in local control, and perhaps in OS. Early data from Japanese centers have shown promising results. In conclusion, this is the first trial to evaluate actively delivered carbon ion beams in patients with locally advanced pancreatic cancer within a dose-escalation strategy. Trial registration: NCT01795274.

[204]

TÍTULO / TITLE: - Aspirin prolongs survival and reduces the number of Foxp3 regulatory T cells in a genetically engineered mouse model of pancreatic cancer.

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

REVISTA / JOURNAL: - Langenbecks Arch Surg. 2013 Oct;398(7):989-996. Epub 2013 Aug 30.

●● Enlace al texto completo (gratis o de pago) [1007/s00423-013-1105-2](#)

AUTORES / AUTHORS: - Plassmeier L; Knoop R; Waldmann J; Kesselring R; Buchholz M; Fichtner-Feigl S; Bartsch DK; Fendrich V

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Philipps University Marburg, Baldingerstrasse, D-35043, Marburg, Germany.

RESUMEN / SUMMARY: - BACKGROUND AND AIMS: Gemcitabine became the reference regimen for advanced pancreatic cancer after a randomized trial showed significant improvement in the median overall survival. Since then, the combination of gemcitabine with a variety of cytotoxic and targeted agents has generally shown no significant survival advantage as compared with gemcitabine alone. Only the addition of erlotinib to gemcitabine resulted in a significant but very small improvement in overall survival, coming along with a very uncomfortable rash in the patients. Therefore, new adjuvant agents with very low toxic levels are needed. In this study, we used a genetically engineered mouse model of pancreatic cancer to evaluate the chemotherapeutic potential of aspirin as an adjuvant agent to gemcitabine. METHODS: Drug treatment was initiated at the age of 3 months. LsL-Kras G12D ; Pdx1-Cre or LsL-Kras G12D ; LsL-Trp53 R172H ; Pdx1-Cre transgenic mice were randomly assigned to receive either mock treatment, gemcitabine, or a combination of gemcitabine and aspirin. All mice were treated until death. The effect of aspirin was evaluated by histopathological analyses and immunostaining. RESULTS: Gemcitabine prolonged overall median survival of LsL-Kras G12D ; LsL-Trp53 R172H ; Pdx1-Cre mice by 31 days as compared to mock-treated animals (median survival, 190 vs. 159 days; p = 0.396).

Addition of aspirin to gemcitabine even extended the survival for ten more days, leading to a prolonged survival by 41 days, reaching virtually statistical significance versus the control group (median survival, 200 vs. 159 days; $p = 0.05$). Furthermore, we found that administration of aspirin in combination with gemcitabine reduced the number of Foxp3⁺ regulatory T cells significantly. CONCLUSION: In conclusion, we identified aspirin as an effective adjuvant agent to gemcitabine in the treatment of PDAC. While fundamental differences in biology suggest the need for caution in equating mouse tumors with their human counterparts, mouse models nevertheless represent an important source of insight regarding human neoplasia. Further studies are necessary to confirm the hypothesis that aspirin might be an effective well-tolerated chemotherapeutic adjuvant agent for pancreatic cancer.

[205]

TÍTULO / TITLE: - Simultaneous knock-down of Bcl-xL and Mcl-1 induces apoptosis through Bax activation in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Biochim Biophys Acta. 2013 Aug 14;1833(12):2980-2987. doi: 10.1016/j.bbamcr.2013.08.006.

●● Enlace al texto completo (gratis o de pago) [1016/j.bbamcr.2013.08.006](#)

AUTORES / AUTHORS: - Takahashi H; Chen MC; Pham H; Matsuo Y; Ishiguro H; Reber HA; Takeyama H; Hines OJ; Eibl G

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA.

RESUMEN / SUMMARY: - Anti-apoptotic Bcl-2 family proteins have been reported to play an important role in apoptotic cell death of human malignancies. The aim of this study was to delineate the mechanism of anti-apoptotic Bcl-2 family proteins in pancreatic cancer (PaCa) cell survival. We first analyzed the endogenous expression and subcellular localization of anti-apoptotic Bcl-2 family proteins in six PaCa cell lines by Western blot. To delineate the functional role of Bcl-2 family proteins, siRNA-mediated knock-down of protein expression was used. Apoptosis was measured by Cell Death ELISA and Hoechst 33258 staining. In the results, the expression of anti-apoptotic Bcl-2 family proteins varied between PaCa cell lines. Mcl-1 knock-down resulted in marked cleavage of PARP and induction of apoptosis. Down-regulation of Bcl-2 or Bcl-xL had a much weaker effect. Simultaneous knock-down of Bcl-xL and Mcl-1 strongly induced apoptosis, but simultaneous knock-down of Bcl-xL/Bcl-2 or Mcl-1/Bcl-2 had no additive effect. The apoptosis-inducing effect of simultaneous knock-down of Bcl-xL and Mcl-1 was associated with translocation of Bax from the cytosol to the mitochondrial membrane, cytochrome c release, and caspase activation. These results demonstrated

that Bcl-xL and Mcl-1 play an important role in pancreatic cancer cell survival. Targeting both Bcl-xL and Mcl-1 may be an intriguing therapeutic strategy in PaCa.

[206]

TÍTULO / TITLE: - Subtype-Specific MEK-PI3 Kinase Feedback as a Therapeutic Target in Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Sep 26.

●● Enlace al texto completo (gratis o de pago) [1158/1535-7163.MCT-13-](#)

[0104](#)

AUTORES / AUTHORS: - Mirzoeva OK; Collisson EA; Schaefer PM; Hann B; Hom YK; Ko AH; Korn WM

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Divisions of 1Gastroenterology and 2Hematology and Oncology, Department of Medicine; and 3Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, California.

RESUMEN / SUMMARY: - Mutations in the KRAS oncogene are dominant features in pancreatic ductal adenocarcinoma (PDA). Because KRAS itself is considered "undruggable," targeting pathways downstream of KRAS are being explored as a rational therapeutic strategy. We investigated the consequences of MAP-ERK kinase (MEK) inhibition in a large PDA cell line panel. Inhibition of MEK activated phosphoinositide 3-kinase in an EGF receptor (EGFR)-dependent fashion and combinations of MEK and EGFR inhibitors synergistically induced apoptosis. This combinatorial effect was observed in the epithelial but not mesenchymal subtype of PDA. RNA expression analysis revealed predictors of susceptibility to the combination, including E-cadherin, HER3, and the miR200-family of microRNAs, whereas expression of the transcription factor ZEB1 was associated with resistance to the drug combination. Knockdown of HER3 in epithelial-type and ZEB1 in mesenchymal-type PDA cell lines resulted in sensitization to the combination of MEK and EGFR inhibitors. Thus, our findings suggest a new, subtype-specific, and personalized therapeutic strategy for pancreatic cancer. Mol Cancer Ther; 12(10); 1-13. ©2013 AACR.

[207]

TÍTULO / TITLE: - Isolated pancreatic tuberculosis mimicking inoperable pancreatic cancer: a diagnostic challenge resolved using endoscopic ultrasound-guided fine-needle aspiration.

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

REVISTA / JOURNAL: - Can J Gastroenterol. 2013 Aug;27(8):445-7.

AUTORES / AUTHORS: - Sportes A; Kpossou R; Bernardin S

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Strasbourg University, France. adrien.sportes@chru-strasbourg.fr

[208]

TÍTULO / TITLE: - A Novel Small-Molecule Inhibitor of Mcl-1 Blocks Pancreatic Cancer Growth In vitro and In vivo.

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

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Sep 9.

●● Enlace al texto completo (gratis o de pago) [1158/1535-7163.MCT-12-0767](#)

AUTORES / AUTHORS: - Abulwerdi F; Liao C; Liu M; Azmi AS; Aboukameel A; Mady AS; Gulappa T; Cierpicki T; Owens S; Zhang T; Sun D; Stuckey JA; Mohammad RM; Nikolovska-Coleska Z

INSTITUCIÓN / INSTITUTION: - 1Pathology, Medical School, University of Michigan.

RESUMEN / SUMMARY: - Using a high throughput screening (HTS) approach, we have identified and validated several small molecule Mcl-1 inhibitors (SMIs). Here we describe a novel selective Mcl-1 SMI inhibitor, 2 (UMI-77), developed by structure-based chemical modifications of the lead compound 1 (UMI-59). We have characterized the binding of UMI-77 to Mcl-1 by using complementary biochemical, biophysical and computational methods, and determined its antitumor activity against panel of pancreatic cancer (PC) cells and in vivo xenograft model. UMI-77 binds to the BH3 binding groove of Mcl-1 with K_i of 490 nM, showing selectivity over other members of anti-apoptotic Bcl-2 members. UMI-77 inhibits cell growth and induces apoptosis in PC cells in a time and dose-dependent manner, accompanied by cytochrome c release and caspase-3 activation. Co-immunoprecipitation experiments revealed that UMI-77 blocks the heterodimerization of Mcl-1/Bax and Mcl-1/Bak in cells, thus antagonizing the Mcl-1 function. The Bax/Bak-dependent induction of apoptosis was further confirmed by using murine embryonic fibroblasts that are Bax and Bak deficient. In an in vivo BxPC-3 xenograft model, UMI-77 effectively inhibited tumor growth. Western blot analysis in tumor remnants revealed enhancement of pro-apoptotic markers and significant decrease of survivin. Collectively, these promising findings demonstrate the therapeutic potential of Mcl-1 inhibitors against PC and warrant further preclinical investigations.

[209]

TÍTULO / TITLE: - Trends in the Treatment of Resectable Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Sep 4.

●● Enlace al texto completo (gratis o de pago) [1007/s11605-013-2335-x](#)

AUTORES / AUTHORS: - Raigani S; Ammori J; Kim J; Hardacre JM

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Division of Surgical Oncology, University Hospitals Seidman Cancer Center, Case Western Reserve University, 11100 Euclid Avenue, Cleveland, OH, 44106, USA.

RESUMEN / SUMMARY: - **BACKGROUND:** Multiple prospective, randomized trials have demonstrated that the addition of adjuvant therapy after surgical resection of pancreatic cancer improves survival compared to surgery alone. However, the optimal type of adjuvant therapy, chemotherapy alone, or chemotherapy combined with chemoradiation therapy remains controversial. Our aim was to examine the treatment trends for surgically resectable (stages I and II) pancreatic cancer in the USA using the National Cancer Database. **METHODS:** The National Cancer Database (NCDB) is a national oncology outcomes database for over 1,500 Commission on Cancer accredited cancer programs. Patients diagnosed with stage I-II pancreatic adenocarcinoma between 2003 and 2010 were selected from the NCDB Hospital Comparison Benchmark Reports. Attention was paid to the initial treatment regimen, such as surgery alone, surgery plus chemotherapy, or surgery plus chemoradiation. In addition, data on hospital setting (teaching hospitals vs. community hospitals) were collected and analyzed. The Cochran-Armitage test for trend was used to assess changes in treatment over time. **RESULTS:** Fifty-nine thousand ninety-four patients with stage I-II pancreatic adenocarcinoma were included in the analysis. Between 2003 and 2010, the use of surgery alone as first course treatment of stage II disease decreased significantly at both teaching hospitals and community hospitals among patients who underwent surgery ($P < 0.0001$ for both cases). In the same period, the use of chemotherapy in addition to surgery as treatment of stage I and II disease increased at least twofold at both hospital settings ($P < 0.0001$ for all cases). Treatment with surgery plus chemoradiation decreased significantly for both stages in both hospital settings ($P < 0.0001$ for all cases). Nonsurgical treatment for stage II disease was surprisingly high and significantly increased over time ($P < 0.001$ for both hospital types), ranging from approximately 30-37 % at teaching hospitals and 39-47 % at community hospitals. **CONCLUSION:** Data from the NCDB from 2003 to 2010 illustrate changes in the adjuvant treatment of pancreatic cancer. The use of chemotherapy alone as adjuvant therapy increased whereas the use of multimodality therapy decreased. In addition, there remains an alarmingly high rate of nonsurgical therapy for stage I and II disease.

[210]

TÍTULO / TITLE: - Design and discovery of novel quinazolinedione-based redox modulators as therapies for pancreatic cancer.

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

REVISTA / JOURNAL: - Biochim Biophys Acta. 2013 Aug 15. pii: S0304-4165(13)00349-8. doi: 10.1016/j.bbagen.2013.08.005.

- Enlace al texto completo (gratis o de pago) [1016/j.bbagen.2013.08.005](https://doi.org/10.1016/j.bbagen.2013.08.005)

AUTORES / AUTHORS: - Pathania D; Sechi M; Palomba M; Sanna V; Berrettini F; Sias A; Taheri L; Neamati N

INSTITUCIÓN / INSTITUTION: - Department of Pharmacology and Pharmaceutical Sciences, University of Southern California, School of Pharmacy, 1985 Zonal Avenue, Los Angeles, CA, USA.

RESUMEN / SUMMARY: - **BACKGROUND:** Altered cellular bioenergetics and oxidative stress are emerging hallmarks of most cancers including pancreatic cancer. Elevated levels of intrinsic reactive oxygen species (ROS) in tumors make them more susceptible to exogenously induced oxidative stress. Excessive oxidative insults overwhelm their adaptive antioxidant capacity and trigger ROS-mediated cell death. Recently, we have discovered a novel class of quinazolinones that exert their cytotoxic effects by modulating ROS-mediated signaling. **METHODS:** Cytotoxic potential was determined by colorimetric and colony formation assays. An XF24 Extracellular Flux Analyzer, and colorimetric and fluorescent techniques were used to assess the bioenergetics and oxidative stress effects, respectively. Mechanism was determined by Western blots. **RESULTS:** Compound 3^a (6-[(2-acetylphenyl)amino]quinazolin-5,8-dione) was identified through a medium throughput screen of ~1000 highly diverse in-house compounds and chemotherapeutic agents for their ability to alter cellular bioenergetics. Further structural optimizations led to the discovery of a more potent analog, 3b (6-[(3-acetylphenyl)amino]quinazolin-5,8-dione) that displayed anti-proliferative activities in low micromolar range in both drug-sensitive and drug-resistant cancer cells. Treatment with 3b causes Akt activation resulting in increased cellular oxygen consumption and oxidative stress in pancreatic cancer cells. Moreover, oxidative stress induced by 3b promoted activation of stress kinases (p38/JNK) resulting in cancer cell death. Treatment with antioxidants was able to reduce cell death confirming ROS-mediated cytotoxicity. **CONCLUSION:** In conclusion, our novel quinazolinones are promising lead compounds that selectively induce ROS-mediated cell death in cancer cells and warrant further preclinical studies. **GENERAL SIGNIFICANCE:** Since 3b (6-[(3-acetylphenyl)amino]quinazolin-5,8-dione) exerts Akt-dependent ROS-mediated cell death, it might provide potential therapeutic options for chemoresistant and Akt-overexpressing cancers.

[211]

TÍTULO / TITLE: - The modified Glasgow Prognostic Score (mGPS) is a good predictor of indication for palliative bypass surgery in patients with unresectable pancreatic and biliary cancers.

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

REVISTA / JOURNAL: - Int J Clin Oncol. 2013 Sep 3.

- Enlace al texto completo (gratis o de pago) [1007/s10147-013-0613-y](https://doi.org/10.1007/s10147-013-0613-y)

AUTORES / AUTHORS: - Ikuta Y; Takamori H; Sakamoto Y; Hashimoto D; Chikamoto A; Kuroki H; Sakata K; Sakamoto K; Hayashi H; Imai K; Nitta H; Hirota M; Kanemitsu K; Beppu T; Baba H

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Kumamoto, 860-8556, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Patients with unresectable pancreatic and biliary cancers sometimes need decompression due to obstruction of the gastrointestinal tract and/or biliary tract. The aim of this study was to determine the prognostic factors associated with an indication for palliative bypass surgery in patients with unresectable pancreatic and biliary cancers. METHODS: Between April 2005 and September 2011, 37 patients with unresectable pancreatic and biliary cancers underwent palliative bypass surgery. Prognostic factors were searched for among clinical characteristics, operation-related factors, and tumor-related factors using a prospective database. RESULTS: The median survival time (MST) of these patients was 4.6 months, with a 6-month survival rate of 40.5 %. A multivariate Cox proportional hazards regression analysis revealed that mGPS >2 was the only independent prognostic factor for bypass surgery. Patients with an mGPS of 2 had an MST of 1.7 months, and they had a significantly worse prognosis than mGPS 0-1 patients with an MST of 6.3 months. CONCLUSIONS: The mGPS is useful for predicting survival after surgical decompression due to gastrointestinal obstruction in patients with unresectable pancreatic and biliary cancers. Patients with a poor mGPS may not be indicated for palliative bypass surgery.

[212]

TÍTULO / TITLE: - Clinical Significance of Serum COL6A3 in Pancreatic Ductal Adenocarcinoma.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Sep 4.

●● Enlace al texto completo (gratis o de pago) [1007/s11605-013-2326-y](#)

AUTORES / AUTHORS: - Kang CY; Wang J; Axell-House D; Soni P; Chu ML; Chipitsyna G; Sarosiek K; Sendekci J; Hyslop T; Al-Zoubi M; Yeo CJ; Arafat HA

INSTITUCIÓN / INSTITUTION: - Departments of Surgery and the Jefferson Pancreatic, Biliary & Related Cancer Center, Thomas Jefferson University, 1015 Walnut St, Suite 618 Curtis, Philadelphia, PA, 19107, USA.

RESUMEN / SUMMARY: - Type VI collagen (COL6) forms a microfibrillar network often associated with type I collagen and constitutes a major component of the desmoplastic reaction in pancreatic ductal adenocarcinoma (PDA). We have demonstrated recently that the alpha3 chain of COL6, COL6A3, is highly expressed in PDA tissue and undergoes tumor-specific alternative splicing. In this study, we investigated the

diagnostic value and clinical significance of circulating COL6A3 protein and mRNA in PDA. COL6A3 levels in sera from patients with PDA (n = 44), benign lesions (n = 46) and age-matched healthy volunteers (n = 30) were analyzed by enzyme-linked immunosorbent assays (ELISA). Predictive abilities of COL6A3 were examined using receiver operating characteristic (ROC) curves from logistic regression models for PDA versus normal or benign serum levels. Expression levels were correlated with clinicopathological parameters. Real-time PCR was used to analyze the presence of COL6A3 mRNA containing alternative spliced exons E3, E4, and E6. Circulating COL6A3 protein levels were significantly elevated in PDA patients when compared to healthy sera (p = 0.0001) and benign lesions (p = 0.0035). The overall area under the ROC was 0.975. Log(COL6A3) alone provided good discrimination between PDA and benign lesions (area under the curve (AUC) = 0.817), but combined with CA19-9 provided excellent discrimination (AUC = 0.904). Interestingly, high COL6A3 serum levels were significantly associated with perineural invasion and cigarette smoking. Combined E3, E4, and E6 serum RNA values provided good sensitivity but low specificity. Our data demonstrate for the first time the potential clinical significance of circulating COL6A3 in the diagnosis of pancreatic malignancy.

[213]

TÍTULO / TITLE: - Vitamin D deficiency and prognostics among patients with pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - J Transl Med. 2013 Sep 8;11(1):206.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1479-5876-11-206](#)

AUTORES / AUTHORS: - Cho M; Peddi PF; Ding K; Chen L; Thomas D; Wang J; Lockhart AC; Tan B; Wang-Gillam A

RESUMEN / SUMMARY: - **BACKGROUND:** The prevalence of vitamin D deficiency among patients with cancer has been previously reported. Because vitamin D is fat soluble, patients with pancreatic adenocarcinoma may have an especially high risk of vitamin D deficiency in association with ongoing and varying degrees of malabsorption. However, little is known about the correlation between vitamin D status and prognosis in these patients. **METHODS:** We conducted a retrospective review of vitamin D status in patients with pancreatic adenocarcinoma who were treated at Siteman Cancer Center. Patients' demographic information, clinical staging at the time of vitamin D assessment, vitamin D levels, and survival data were collected. Vitamin D deficiency was defined as a serum 25-hydroxyvitamin D (25[OH]D) level of less than 20 ng/mL, and vitamin D insufficiency was defined as a 25(OH)D level of between 20 ng/mL and 30 ng/mL. **RESULTS:** Between December 2007 and June 2011, 178 patients with pancreatic adenocarcinoma had their vitamin D levels checked at the time of initial visit at this center. Of these 178 patients, 87 (49%) had vitamin D deficiency, and 44

(25%) had vitamin D insufficiency. The median 25(OH)D level was significantly lower among nonwhite patients and among patients with stage I and II disease. A 25(OH)D level of less than 20 ng/mL was found to be associated with poor prognosis ($p = 0.0019$) in patients with stage III and IV disease. CONCLUSIONS: Vitamin D insufficiency and deficiency were prevalent among patients with pancreatic adenocarcinoma. The vitamin D level appears to be prognostic for patients with advanced pancreatic adenocarcinoma, and its effects should be further examined in a prospective study.

[214]

TÍTULO / TITLE: - miR-204 mediated loss of Myeloid cell leukemia-1 results in pancreatic cancer cell death.

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

REVISTA / JOURNAL: - Mol Cancer. 2013 Sep 11;12(1):105.

●● Enlace al texto completo (gratis o de pago) [1186/1476-4598-12-105](#)

AUTORES / AUTHORS: - Chen Z; Sangwan V; Banerjee S; Mackenzie T; Dudeja V; Li X; Wang H; Vickers SM; Saluja AK

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is one of the most lethal human malignancies, with an all-stage 5-year survival of <5%, mainly due to lack of effective available therapies. Cancer cell survival is dependent upon up-regulation of the pro-survival response, mediated by anti-apoptotic proteins such as Mcl-1. RESULTS: Here we show that over-expression of Mcl-1 in pancreatic patient tumor samples are linked to advancement of the disease. We have previously shown that triptolide, a diterpene triepoxide, is effective both in vitro and in vivo, in killing pancreatic cancer cells. Decrease of Mcl-1 levels, either by siRNA or by treatment with triptolide results in cell death. Using pancreatic cancer cell lines, we have shown that miR-204, a putative regulator of Mcl-1, is repressed in cancer cell lines compared to normal cells. Over-expression of miR-204, either by a miR-204 mimic, or by triptolide treatment results in a decrease in Mcl-1 levels, and a subsequent decrease in cell viability. Using luciferase reporter assays, we confirmed the ability of miR-204 to down-regulate Mcl-1 by directly binding to the Mcl-1 3' UTR. Using human xenograft samples treated with Minnelide, a water soluble variant of triptolide, we have shown that miR-204 is up-regulated and Mcl-1 is down-regulated in treated vs. control tumors. CONCLUSION: Triptolide mediated miR-204 increase causes pancreatic cancer cell death via loss of Mcl-1.

[215]

TÍTULO / TITLE: - Pancreatic cystic neoplasm: surgery or conservative.

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

REVISTA / JOURNAL: - Clin Gastroenterol Hepatol. 2013 Aug 23. pii: S1542-3565(13)01233-0. doi: 10.1016/j.cgh.2013.08.031.

●● Enlace al texto completo (gratis o de pago) 1016/j.cgh.2013.08.031

AUTORES / AUTHORS: - Talukdar R; Reddy DN

INSTITUCIÓN / INSTITUTION: - Asian Institute of Gastroenterology, Hyderabad, India; Asian Healthcare Foundation, Hyderabad, India.

RESUMEN / SUMMARY: - Pancreatic cystic neoplasms (PCNs) are a heterogeneous group of tumors with distinct biological features. These neoplasms are now being recognized more frequently due to advances in cross-sectional imaging and increasing awareness. Guidelines for treatment of the common and clinically important PCNs have been frequently revised in view of the continuing controversies and evolving clinical data. This review summarizes the management approaches of the common and clinically important PCNs based on current evidence and guidelines.

[216]

TÍTULO / TITLE: - Breast cancer metastases to the pancreas.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Oct;17(10):1826-31. doi: 10.1007/s11605-013-2291-5. Epub 2013 Aug 6.

●● Enlace al texto completo (gratis o de pago) 1007/s11605-013-2291-5

AUTORES / AUTHORS: - Bednar F; Scheiman JM; McKenna BJ; Simeone DM

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Michigan, Ann Arbor, MI, USA.

RESUMEN / SUMMARY: - INTRODUCTION: The pancreas can serve as the destination for metastatic spread of malignancies from multiple organ sites. Breast cancer metastases to the pancreas are part of this spectrum and surgeons evaluate such patients as part of their practice. Uniform clinical guidelines for these cases do not exist and care is primarily driven by the personal experience of the treating surgeon. DISCUSSION: We present two patients with breast cancer metastases to their pancreas and review their workup and clinical management in light of our experience and the existing published literature. We propose that metastatic disease to the pancreas has to remain in the differential diagnosis for any patient with a new pancreatic mass and prior cancer history. Surgical resection is a viable treatment option for patients with isolated metastatic disease to the pancreas if the underlying biology of the metastatic tumor is favorable.

[217]

TÍTULO / TITLE: - Synchronous adenocarcinoma of the gall bladder and pancreas in a young woman.

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

REVISTA / JOURNAL: - Trop Gastroenterol. 2013 Jan-Mar;34(1):50-2.

AUTORES / AUTHORS: - Agarwal N; Kumar S; Sharma S

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, India. drnitinagarwal76@gmail.com

[218]

TÍTULO / TITLE: - Spleen preserving distal pancreatectomy for a large papillary cystic and solid tumor of the pancreas.

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

REVISTA / JOURNAL: - Trop Gastroenterol. 2012 Oct-Dec;33(4):287-9.

AUTORES / AUTHORS: - Shindholimath V; Thinagaran K; Nagaraj A; Rao N; Yenni VV

INSTITUCIÓN / INSTITUTION: - Department of Surgery, PES Institute of Medical Sciences and Research, Kuppam, 517 425, Dist Chittoor, Andhra Pradesh. vishwashi@rediff.com

[219]

TÍTULO / TITLE: - Total laparoscopic pancreaticoduodenectomy.

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

REVISTA / JOURNAL: - JSLS. 2013 Apr-Jun;17(2):188-93. doi: 10.4293/108680813X13654754534792.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[4293/108680813X13654754534792](https://doi.org/10.4293/108680813X13654754534792)

AUTORES / AUTHORS: - Jacobs MJ; Kamyab A

INSTITUCIÓN / INSTITUTION: - Department of Surgery, St. John Providence Health, Southfield, MI, USA. mjjacobsm@gmail.com

RESUMEN / SUMMARY: - INTRODUCTION: Total laparoscopic pancreaticoduodenectomy (TLPD) remains one of the most advanced laparoscopic procedures. Owing to the evolution in laparoscopic technology and instrumentation within the past decade, laparoscopic pancreaticoduodenectomy is beginning to gain wider acceptance. METHODS: Data were collected for all patients who underwent a TLPD at our institution. Preoperative evaluation consisted of computed tomography scan with pancreatic protocol and selective use of magnetic resonance imaging and/or endoscopic ultrasonography. The TLPD was done with 6 ports on 3 patients and 5 ports in 2 patients and included a celiac, periportal, peripancreatic, and periduodenal lymphadenectomy. Pancreatic stents were used in all 5 cases, and intestinal continuity was re-established by intracorporeal anastomoses. RESULTS: Five patients underwent a TLPD for suspicion of a periampullary tumor. There were 3 women and 2 men with a mean age of 60 years and a mean body mass index of 32.8. Intraoperatively, the mean operative time was 9 hours 48 minutes, with a mean blood loss of 136 mL.

Postoperatively, there were no complications and a mean length of stay of 6.6 days. There was no lymph node involvement in 4 out of 5 specimens. The pathological results included intraductal papillary mucinous neoplasm in 2 patients, pancreatic adenocarcinoma in 1 patient (R0 resection), benign 4-cm periampullary adenoma in 1 patient, and a somatostatin neuroendocrine carcinoma in 1 patient (R0, N1). CONCLUSION: TLPD is a viable alternative to the standard Whipple procedure. Our early experience suggests decreased length of stay, quicker recovery, and improved quality of life. Complication rates appear to be improved or equivalent.

[220]

TÍTULO / TITLE: - Intrahepatic rupture of hepatic hydatid cyst with impacted hydatid membranes at ampulla of Vater presenting as acute pancreatitis.

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

REVISTA / JOURNAL: - Trop Gastroenterol. 2013 Jan-Mar;34(1):43-4.

AUTORES / AUTHORS: - Chaudhary A; Upadhyaya AC; Kankanala VV; Kumar A; Joshi N; Kumar M; Harwani Y; Choudeswari RP

INSTITUCIÓN / INSTITUTION: - Department of Medical Gastroenterology, Nizam's Institute of Medical Sciences, Panjagutta, Hyderabad, Andhra Pradesh, India.

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[221]

TÍTULO / TITLE: - Diagnostic evaluation of solid pancreatic masses.

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

REVISTA / JOURNAL: - Curr Gastroenterol Rep. 2013 Oct;15(10):347. doi: 10.1007/s11894-013-0347-z.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s11894-013-0347-z](#)

AUTORES / AUTHORS: - Tokar JL; Walia R

INSTITUCIÓN / INSTITUTION: - Fox Chase Cancer Center, Philadelphia, PA, USA,

Jeffrey.Tokar@fccc.edu.

RESUMEN / SUMMARY: - Determining the etiology of a solid pancreatic lesion is a critical first step toward developing an appropriate treatment plan for patients with a benign or malignant pancreatic mass. Technological advances in cross-sectional and endoscopic imaging modalities offer pancreatic imaging options with degrees of resolution that were not available even 15-20 years ago. In most cases, the nature of a solid pancreatic mass can be determined using computerized tomography, magnetic resonance imaging, and endoscopic ultrasound with fine-needle aspiration. Knowledge about the basics of these modalities, as well as their strengths and limitations, plays an important role in understanding how patients with solid pancreatic masses should be evaluated.

[222]

TÍTULO / TITLE: - Inhibiting signal transducer and activator of transcription-3 increases response to gemcitabine and delays progression of pancreatic cancer.

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

REVISTA / JOURNAL: - Mol Cancer. 2013 Sep 11;12(1):104.

●● Enlace al texto completo (gratis o de pago) [1186/1476-4598-12-104](#)

AUTORES / AUTHORS: - Venkatasubbarao K; Peterson L; Zhao S; Hill P; Cao L; Zhou Q; Nawrocki ST; Freeman JW

RESUMEN / SUMMARY: - BACKGROUND: Among the solid tumors, human pancreatic ductal adenocarcinoma (PDAC) has the worst prognosis. Gemcitabine is the standard first line of therapy for pancreatic cancer but has limited efficacy due to inherent or rapid development of resistance and combining EGFR inhibitors with this regimen results in only a modest clinical benefit. The goal of this study was to identify molecular targets that are activated during gemcitabine therapy alone or in combination with an EGFR inhibitor. METHODS: PDAC cell lines were used to determine molecular changes and rates of growth after treatment with gemcitabine or an EGFR inhibitor, AG1478, by Western blot analysis and MTT assays respectively. Flow cytometric analysis was performed to study the cell cycle progression and rate of apoptosis after gemcitabine treatment. ShRNA was used to knockdown STAT3. An in vivo orthotopic animal model was used to evaluate STAT3 as a target.

Immunohistochemical analysis was performed to analyze Ki67 and STAT3 expression in tumors. RESULTS: Treatment with gemcitabine increased the levels of EGFR^{Tyr1068} and ERK phosphorylation in the PDAC cell lines tested. The constitutive STAT3^{Tyr705} phosphorylation observed in PDAC cell lines was not altered by treatment with gemcitabine. Treatment of cells with gemcitabine or AG1478 resulted in differential rate of growth inhibition. AG1478 efficiently blocked the phosphorylation of EGFR^{Tyr1068} and inhibited the phosphorylation of down-stream effectors AKT and ERKs, while STAT3^{Tyr705} phosphorylation remained unchanged. Combining these two agents neither induced synergistic growth suppression nor inhibited STAT3^{Tyr705} phosphorylation, thus prompting further studies to assess whether targeting STAT3 improves the response to gemcitabine or AG1478. Indeed, knockdown of STAT3 increased sensitivity to gemcitabine by inducing pro-apoptotic signals and by increasing G1 cell cycle arrest. However, knockdown of STAT3 did not enhance the growth inhibitory potential of AG1478. In vivo orthotopic animal model results show that knockdown of STAT3 caused a significant reduction in tumor burden and delayed tumor progression with increased response to gemcitabine associated with a decrease in the Ki-67 positive cells. CONCLUSIONS: This study suggests that STAT3 should be considered an important molecular target for therapy of PDAC for enhancing the response to gemcitabine.

[223]

TÍTULO / TITLE: - Trends in Racial Disparities in Pancreatic Cancer Surgery.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Sep 4.

●● Enlace al texto completo (gratis o de pago) [1007/s11605-013-2304-4](#)

AUTORES / AUTHORS: - Shah A; Chao KS; Ostbye T; Castleberry AW; Pietrobon R; Gloor B; Clary BM; White RR; Worni M

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Columbia University Medical Center, New York, NY, USA.

RESUMEN / SUMMARY: - OBJECTIVES: We tested three hypotheses: (1) blacks with pancreatic cancer are recommended surgical resection less often than whites; (2) when recommended surgical resection, blacks refuse surgery more often than whites; and lastly, (3) racial differences in refusal of surgical resection have decreased over time. METHODS: A retrospective cohort study was conducted on patients with potentially resectable, nonmetastatic pancreatic adenocarcinoma of the Surveillance, Epidemiology, and End Results registry from 1988 to 2009. Univariate and multivariable logistic regression analyses were performed to assess whether differences in the proportion of whites versus blacks refusing surgery among patients recommended for resection changed over time. RESULTS: A total of 35,944 patients were included; most were white (87.6 %). After adjusting for covariates including tumor stage, pancreatic cancer resection was less often recommended to and performed in blacks compared with whites (adjusted odds ratio (aOR) 0.88, 95 % confidence interval (CI) 0.82-0.95; aOR 0.83, 95 % CI 0.76-0.91, respectively). Blacks also underwent surgical resection less often when surgery was recommended (aOR 0.73, 95 % CI 0.64-0.85). Racial disparities in surgery recommendation and its performance did not decrease from 1988 to 2009. In multivariable adjusted analyses, blacks refused surgery more often when it was recommended (aOR in 1988 4.75, 95 % CI 2.51-9.01); this disparity decreased over time (aOR 0.93 per year, 95 % CI 0.89-0.97). CONCLUSIONS: Although racial disparities in pancreatic cancer surgery refusal have diminished over the past two decades, significant disparities in the recommendation and performance of surgery persist. It is likely that both provider- and patient-level factors have a substantial impact on surgery recommendation and its acceptance. The identification of such factors is critical to design a framework for eliminating disparities in cancer-directed surgery for pancreatic cancer.

[224]

TÍTULO / TITLE: - Irreversible electroporation of locally advanced pancreatic head adenocarcinoma.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Oct;17(10):1850-6. doi: 10.1007/s11605-013-2309-z. Epub 2013 Aug 9.

●● Enlace al texto completo (gratuito o de pago) [1007/s11605-013-2309-z](#)

AUTORES / AUTHORS: - Martin RC

INSTITUCIÓN / INSTITUTION: - University of Louisville, Louisville, KY, USA,
Robert.Martin@louisville.edu.

RESUMEN / SUMMARY: - Irreversible electroporation of locally advanced pancreatic adenocarcinoma has been used to palliate appropriate patients with locally advanced pancreatic adenocarcinoma. The setting was at a university tertiary care center. Subjects are patients with locally advanced pancreatic adenocarcinoma who have undergone appropriate induction chemotherapy for at least 3 to 4 months in duration. Technique of open irreversible electroporation of locally advanced pancreatic adenocarcinoma is described. The technique of open irreversible electroporation with continuous intraoperative ultrasound imaging and consideration of intraoperative navigational system is described. Irreversible electroporation of locally advanced pancreatic adenocarcinoma is feasible for locally advanced unresectable pancreatic cancer.

[225]

TÍTULO / TITLE: - Schwannomatosis presenting as pancreatic and submandibular gland schwannoma.

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

REVISTA / JOURNAL: - Pathol Res Pract. 2013 Aug 27. pii: S0344-0338(13)00213-6. doi: 10.1016/j.prp.2013.08.009.

●● Enlace al texto completo (gratuito o de pago) [1016/j.prp.2013.08.009](#)

AUTORES / AUTHORS: - Val-Bernal JF; Mayorga M; Sedano-Tous MJ

INSTITUCIÓN / INSTITUTION: - Department of Anatomical Pathology, Marques de Valdecilla University Hospital, Medical Faculty, University of Cantabria and IFIMAV, Santander, España. Electronic address: apavbj@humv.es.

RESUMEN / SUMMARY: - Schwannomatosis is a well-established third form of neurofibromatosis, characterized by the presence of multiple non-vestibular, non-intradermal schwannomas, often associated with chronic pain. Herein, we report a 41-year-old man with a history of paternal neurofibromatosis 1, who presented with partially cystic tumors in the pancreas and in the right submandibular gland. Besides, he complained of neuropathic pain in the right inguinal and suprapubic area. Magnetic resonance imaging revealed multiple intradural-extramedullary tumors at the cervical, thoracic and lumbar spinal canal, suggestive of schwannomas. The vestibular nerves were not involved. Pathological examination of the glandular tumors disclosed benign schwannomas. These tumors had substantial myxoid stroma and prominent cystic

change, and showed a mosaic pattern of loss of INI1/SMARCB1 expression by immunohistochemistry. Later, the patient developed three nodules in the right lung which were interpreted as schwannomas. To our knowledge, this is the first report of schwannomatosis presenting as pancreatic and salivary gland schwannomas.

[226]

TÍTULO / TITLE: - To Cease or 'De-cyst'? The Evaluation and Management of Pancreatic Cystic Lesions.

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

REVISTA / JOURNAL: - Curr Gastroenterol Rep. 2013 Oct;15(10):348. doi: 10.1007/s11894-013-0348-y.

●● Enlace al texto completo (gratis o de pago) [1007/s11894-013-0348-y](#)

AUTORES / AUTHORS: - Enestvedt BK; Ahmad N

INSTITUCIÓN / INSTITUTION: - Oregon Health & Science University, 3181 SW Sam Jackson Park Rd, L461, Portland, OR, 97239, USA, brintha.e@gmail.com.

RESUMEN / SUMMARY: - Due to the widespread use of cross-sectional imaging and advances in imaging technology, pancreatic cystic lesions are increasingly being detected. The diagnosis and management of such cysts remains challenging and continues to evolve. Different pancreatic cyst types have varying malignant potential. Thus, accurate cyst characterization is essential to appropriate management; the most clinically important distinction is differentiating mucinous lesions, which have malignant potential and may benefit from surgical resection, from non-mucinous cystic lesions. Endoscopic ultrasound with fine needle aspiration with cytologic, chemical, and tumor marker analysis appears to be the best currently available method for accurately characterizing a cyst's malignant potential, and therefore impacts the most important management decision for a pancreatic cyst-continued surveillance or surgical resection.

[227]

TÍTULO / TITLE: - An efficient pancreatic cyst identification methodology using natural language processing.

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

REVISTA / JOURNAL: - Stud Health Technol Inform. 2013;192:822-6.

AUTORES / AUTHORS: - Mehrabi S; Schmidt CM; Waters JA; Beesley C; Krishnan A; Kesterson J; Dexter P; Al-Haddad MA; Tierney WM; Palakal M

INSTITUCIÓN / INSTITUTION: - School of Informatics, Indiana University, Indianapolis, IN, USA.

RESUMEN / SUMMARY: - Pancreatic cancer is one of the deadliest cancers, mostly diagnosed at late stages. Patients with pancreatic cysts are at higher risk of developing

cancer and their surveillance can help to diagnose the disease in earlier stages. In this retrospective study we collected a corpus of 1064 records from 44 patients at Indiana University Hospital from 1990 to 2012. A Natural Language Processing (NLP) system was developed and used to identify patients with pancreatic cysts. NegEx algorithm was used initially to identify the negation status of concepts that resulted in precision and recall of 98.9% and 89% respectively. Stanford Dependency parser (SDP) was then used to improve the NegEx performance resulting in precision of 98.9% and recall of 95.7%. Features related to pancreatic cysts were also extracted from patient medical records using regex and NegEx algorithm with 98.5% precision and 97.43% recall. SDP improved the NegEx algorithm by increasing the recall to 98.12%.

[228]

TÍTULO / TITLE: - Complications of endoscopic ultrasound fine needle aspiration on pancreatic cystic lesions: Final results from a large prospective multicenter study.

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

REVISTA / JOURNAL: - Dig Liver Dis. 2013 Sep 17. pii: S1590-8658(13)00419-2. doi: 10.1016/j.dld.2013.08.134.

●● Enlace al texto completo (gratis o de pago) [1016/j.dld.2013.08.134](#)

AUTORES / AUTHORS: - Tarantino I; Fabbri C; Di Mitri R; Pagano N; Barresi L; Mocciaro F; Maimone A; Curcio G; Repici A; Traina M

INSTITUCIÓN / INSTITUTION: - Gastroenterology Department, ISMETT/UPMC (Mediterranean Institute for Transplantation and Advanced Specialized Therapies/University of Pittsburgh Medical Center in Italy), Palermo, Italy. Electronic address: itarantino@ismett.edu.

RESUMEN / SUMMARY: - BACKGROUND: Endoscopic ultrasound-guided fine needle aspiration of pancreatic cystic lesions has been reported to have a higher complication rate than that of solid lesions, but the real complication rate is unknown. Aim of the study was to identify the complication rate of endoscopic ultrasound-guided fine needle aspiration and related risk factors. METHODS: Prospective multicenter study at four referral centres. Data were collected from January 2010 to July 2012, searching for all adverse events related to guided fine needle aspiration. All complications occurring up to day 90 were recorded. RESULTS: 298 patients (43.9% male, mean age 63.2+/-15.4 years) underwent endoscopic ultrasound-guided needle aspiration of pancreatic cystic lesions. Mean size was 34.1+/-9mm. Adverse events occurred in 18 patients (6%): mild complications in 12/18 (66.6%), and moderate complications in 6/18 (33.3%). Seven were immediate, 6 early, and 5 late. All resolved with medical therapy. CONCLUSIONS: Endoscopic ultrasound-guided fine needle aspiration of pancreatic cystic lesions has been found to be associated with a higher complication rate than for solid lesions; however, the risk rate is acceptable considering the

complication grade and the important diagnostic role of the technique in the management of pancreatic cystic lesions.

[229]

TÍTULO / TITLE: - The use of targeted therapies in pancreatic neuroendocrine tumours: patient assessment, treatment administration, and management of adverse events.

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

REVISTA / JOURNAL: - Ther Adv Med Oncol. 2013 Sep;5(5):286-300. doi: 10.1177/1758834013501016.

- Enlace al texto completo (gratis o de pago) [1177_1758834013501016](#) [pii]
- Enlace al texto completo (gratis o de pago) [1177/1758834013501016](#)

AUTORES / AUTHORS: - Cummins M; Pavlakis N

INSTITUCIÓN / INSTITUTION: - Director of Nursing, Northern Cancer Institute, 49 Frenchs Forest Road, Frenchs Forest, NSW, 2086, Australia.

RESUMEN / SUMMARY: - Together with the use of novel oral targeted therapies, a multidisciplinary approach can be used to effectively treat patients with advanced pancreatic neuroendocrine tumours (pNETs). Here we review the integration of the oncology nurse to the newly developed oral treatment setting for patients with pNETs. From the outset, the nurse must be involved in various processes, including performance of baseline assessments (e.g. blood pathology, cardiac and lung function testing, patient history) and general medical observations, treatment administration, dietary guidance, evaluation of comorbidities, and review of concomitant medications. Patient education and establishment of a strong partnership in care before the start of pNET therapy ultimately increase treatment adherence and reduce potential toxicities. Regular review of general patient status and disease progression and continuous monitoring of adverse events also help enhance treatment outcomes and subsequently improve quality of life. Nurses' knowledge of agent-specific toxicities and prompt, proactive management is a critical aspect of care. In essence, as the pNET treatment landscape evolves, the role of the healthcare professional in overall patient care must shift accordingly.

[230]

TÍTULO / TITLE: - Molecular diagnostics of pancreatic cysts.

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

REVISTA / JOURNAL: - Langenbecks Arch Surg. 2013 Sep 26.

- Enlace al texto completo (gratis o de pago) [1007/s00423-013-1116-z](#)

AUTORES / AUTHORS: - Matthaehi H; Feldmann G; Lingohr P; Kalff JC

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Bonn, Sigmund-Freud-Str. 25, 53127, Bonn, Germany, hannomatthaehi@gmail.com.

RESUMEN / SUMMARY: - INTRODUCTION: Due to an extensive use of modern imaging, incidental pancreatic cysts are increasingly diagnosed these days. Fortunately, comprehensive research over the past years has remarkably improved our pathogenetic and clinical understanding of pancreatic cysts that, as we know, are in majority harmless. However, mucinous cysts including intraductal papillary mucinous neoplasms, mucinous cystic neoplasms, as well as solid pseudopapillary neoplasms harbor relevant potential for developing into a lethal invasive cancer and may therefore require immediate surgical resection or at least close surveillance. In order to allow an optimized clinical management, it is crucial to gather reliable information about entity as well as biologic behavior of every cyst detected. Unfortunately, in the absence of reliable biomarkers and by just applying currently available diagnostic means such as clinical and radiologic criteria or cyst fluid cytology, there is still a risk for incorrect preoperative diagnoses. This may be followed by inappropriate treatment possibly resulting in severe morbidity or even mortality. OBJECTIVE: In this review article, we summarize some of the salient recent advances in molecular diagnostics of pancreatic cysts. Herein, we put particular focus on the emerging field of biomarker research in pancreatic cyst fluid based on protein, DNA, and microRNA analyses.

[231]

TÍTULO / TITLE: - IGF-1 receptor and IGF binding protein-3 might predict prognosis of patients with resectable pancreatic cancer.

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

REVISTA / JOURNAL: - BMC Cancer. 2013 Aug 21;13(1):392. doi: 10.1186/1471-2407-13-392.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-392](#)

AUTORES / AUTHORS: - Hirakawa T; Yashiro M; Murata A; Hirata K; Kimura K; Amano R; Yamada N; Nakata B; Hirakawa K

INSTITUCIÓN / INSTITUTION: - Department of Surgical Oncology, Osaka City University Graduate School of Medicine, 1-4-3 Asahi-machi, Osaka, Abeno-ku, Japan.
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RESUMEN / SUMMARY: - BACKGROUND: The present study aimed to elucidate the clinicopathologic role of insulin-like growth factor-1 receptor (IGF1R) and IGF binding protein-3 (IGFBP3) in patients with pancreatic cancer. The function of IGFBP3 is controversial, because both inhibition and facilitation of the action of IGF as well as IGF-independent effects have been reported. In this study, IGF1R and IGFBP3 expression was examined, and their potential roles as prognostic markers in patients with pancreatic cancer were evaluated. METHODS: Clinicopathological features of 122 patients with curatively resected pancreatic cancer were retrospectively reviewed, and expression of IGF1R and IGFBP3 was immunohistochemically analyzed. RESULTS:

Expression of IGF1R and IGFBP3 was observed in 50 (41.0%) and 37 (30.3%) patients, respectively. IGF1R expression was significantly associated with histological grade ($p = 0.037$). IGFBP3 expression had a significant association with tumor location ($p = 0.023$), and a significant inverse association with venous invasion ($p = 0.037$). Tumors with IGF1R-positive and IGFBP3-negative expression ($n = 32$) were significantly frequently Stage II and III ($p = 0.011$). The prognosis for IGF1R positive patients was significantly poorer than that for IGF1R negative patients ($p = 0.0181$). IGFBP3 protein expression did not correlate significantly with patient survival. The subset of patients with both positive IGF1R and negative IGFBP3 had worse overall survival (8.8 months versus 12.6 months, respectively, $p < 0.001$). CONCLUSION: IGF1R signaling might be associated with tumor aggressiveness, and IGFBP3 might show antiproliferative effects in pancreatic cancer. Both high IGF1R expression and low IGFBP3 expression represent useful prognostic markers for patients with curatively resected pancreatic cancer.

[232]

TÍTULO / TITLE: - Isolated caudate lobectomy with pancreatoduodenectomy for a bile duct cancer.

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

REVISTA / JOURNAL: - Langenbecks Arch Surg. 2013 Sep 13.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s00423-013-1110-5](#)

AUTORES / AUTHORS: - Sano T; Shimizu Y; Senda Y; Komori K; Ito S; Abe T; Kinoshita T; Nimura Y

INSTITUCIÓN / INSTITUTION: - Hepatobiliary and Pancreatic Surgery Division, Department of Gastroenterological Surgery, Aichi Cancer Center Hospital, Nagoya, Japan, tsusano@aichi-cc.jp.

RESUMEN / SUMMARY: - BACKGROUND: In patients with distal bile duct cancer involving the hepatic hilus, a major hepatectomy concomitant with pancreatoduodenectomy (HPD) is sometimes ideal to obtain a cancer-free resection margin. However, the surgical invasiveness of HPD is considerable. PATIENTS AND METHODS: We present our treatment option for patients with distal bile duct cancer showing mucosal spreading to the hepatic hilum associated with impaired liver function. To minimize resection volume of the liver, an isolated caudate lobectomy (CL) with pancreatoduodenectomy (PD) using an anterior liver splitting approach is presented. Liver transection lines and bile duct resection points correspond complete with our standard right and left hemihepatectomies with CL for perihilar cholangiocarcinoma. RESULTS: Total operation time was 765 min, and pedicle occlusion time was 124 min, respectively. Although the proximal mucosal cancer extension was identified at both the right and the left hepatic ducts, all resection margins were negative for cancer. CONCLUSIONS: Isolated CL with PD is an alternative radical treatment option for bile duct cancer patients with impaired liver function.

[233]

TÍTULO / TITLE: - Influence of preoperative anti-cancer therapy on resectability and perioperative outcomes in patients with pancreatic cancer: Project study by the Japanese Society of Hepato-Biliary-Pancreatic Surgery.

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

REVISTA / JOURNAL: - J Hepatobiliary Pancreat Sci. 2013 Aug 1. doi: 10.1002/jhbp.15.

●● Enlace al texto completo (gratis o de pago) [1002/jhbp.15](#)

AUTORES / AUTHORS: - Motoi F; Unno M; Takahashi H; Okada T; Wada K; Sho M; Nagano H; Matsumoto I; Satoi S; Murakami Y; Kishiwada M; Honda G; Kinoshita H; Baba H; Hishinuma S; Kitago M; Tajima H; Shinchi H; Takamori H; Kosuge T; Yamaue H; Takada T

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterological Surgery, Department of Surgery, Tohoku University Graduate School of Medicine, 1-1 Seiryomachi, Aoba-ku, Sendai, 980-8574, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Little is known about the effects of neoadjuvant therapy on outcomes in patients with pancreatic cancer. This study evaluated the effects of neoadjuvant therapy on resectability and perioperative outcomes. METHODS: A total of 992 patients were enrolled, with 971 deemed eligible. Of these, 582 had resectable tumors and 389 had borderline resectable tumors, and 388 patients received neoadjuvant therapy. Demographic characteristics and peri- and postoperative parameters were assessed by a questionnaire survey. RESULTS: The R0 rate was significantly higher in patients with resectable tumors who received neoadjuvant therapy than in those who underwent surgery first, but no significant difference was noted in patients with borderline resectable tumors. Operation time was significantly longer and blood loss was significantly greater in patients who received neoadjuvant therapy than in those who underwent surgery first, but there were no significant differences in specific complications and mortality rates. The node positivity rate was significantly lower in the neoadjuvant than in the surgery-first group, indicating that the former had significantly lower stage tumors. CONCLUSIONS: Neoadjuvant therapy may not increase the mortality and morbidity rate and may be able to increase the chance for curative resection against resectable tumor.

[234]

TÍTULO / TITLE: - Effects of interportal error on dose distribution in patients undergoing breath-holding intensity-modulated radiotherapy for pancreatic cancer: evaluation of a new treatment planning method.

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

REVISTA / JOURNAL: - J Appl Clin Med Phys. 2013 Sep 6;14(5):4252. doi: 10.1120/jacmp.v14i5.4252.

AUTORES / AUTHORS: - Takakura T; Nakamura M; Shibuya K; Nakata M; Nakamura A; Matsuo Y; Shiinoki T; Higashimura K; Teshima T; Hiraoka M

INSTITUCIÓN / INSTITUTION: - Kyoto University Hospital, Osaka University.

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RESUMEN / SUMMARY: - In patients with pancreatic cancer, intensity-modulated radiotherapy (IMRT) under breath holding facilitates concentration of the radiation dose in the tumor, while sparing the neighboring organs at risk and minimizing interplay effects between movement of the multileaf collimator and motion of the internal structures. Although the breath-holding technique provides high interportal reproducibility of target position, dosimetric errors caused by interportal breath-holding positional error have not been reported. Here, we investigated the effects of interportal breath-holding positional errors on IMRT dose distribution by incorporating interportal positional error into the original treatment plan, using random numbers in ten patients treated for pancreatic cancer. We also developed a treatment planning technique that shortens breath-holding time without increasing dosimetric quality assurance workload. The key feature of our proposed method is performance of dose calculation using the same optimized fluence map as the original plan, after dose per fraction in the original plan was cut in half and the number of fractions was doubled. Results confirmed that interportal error had a negligible effect on dose distribution over multiple fractions. Variations in the homogeneity index and the dose delivered to 98%, 2%, and 50% of the volume for the planning target volume, and the dose delivered to 1 cc of the volume for the duodenum and stomach were +/-1%, on average, in comparison with the original plan. The new treatment planning method decreased breath-holding time by 33%, and differences in dose-volume metrics between the original and the new treatment plans were within +/- 1%. An additional advantage of our proposed method is that interportal errors can be better averaged out; thus, dose distribution in the proposed method may be closer to the planned dose distribution than with the original plans.

[235]

TÍTULO / TITLE: - Predictors of stage and the application of curative-intent surgery in pancreatic cancer: a population-based analysis from the Arkansas Cancer Registry.

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

REVISTA / JOURNAL: - J Ark Med Soc. 2013 Aug;110(2):43-5.

AUTORES / AUTHORS: - Owens P; Henry-Tillman R; Badgwell B

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA.

RESUMEN / SUMMARY: - BACKGROUND: The purpose of this study was to describe the characteristics of pancreatic cancer subjects within the state of Arkansas. METHODS: Pancreatic cancer patients diagnosed from 5/1997 to 12/2007 were identified from the Arkansas Cancer Registry. Analysis was performed to identify variables associated with

advanced-stage and curative-intent surgery. RESULTS: For 3,227 subjects, only grade was associated with advanced stage pancreatic cancer. Age > 80, pancreatic cancer site not specified, and grade were associated with curative-intent surgery. CONCLUSIONS: Studies utilizing the Arkansas Cancer Registry are feasible and can identify variables associated with stage and treatment.

[236]

TÍTULO / TITLE: - Serum carbohydrate antigen 19-9 represents a marker of response to neoadjuvant therapy in patients with borderline resectable pancreatic cancer.

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

REVISTA / JOURNAL: - HPB (Oxford). 2013 Aug 29. doi: 10.1111/hpb.12154.

●● Enlace al texto completo (gratis o de pago) 1111/hpb.12154

AUTORES / AUTHORS: - Tzeng CW; Balachandran A; Ahmad M; Lee JE; Krishnan S; Wang H; Crane CH; Wolff RA; Varadhachary GR; Pisters PW; Aloia TA; Vauthey JN; Fleming JB; Katz MH

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

RESUMEN / SUMMARY: - OBJECTIVES: The purpose of this study was to determine the relationship between carbohydrate antigen (CA) 19-9 levels and outcome in patients with borderline resectable pancreatic cancer treated with neoadjuvant therapy (NT). METHODS: This study included all patients with borderline resectable pancreatic cancer, a serum CA 19-9 level of ≥ 40 U/ml and bilirubin of ≤ 2 mg/dl, in whom NT was initiated at one institution between 2001 and 2010. The study evaluated the associations between pre- and post-NT CA 19-9, resection and overall survival. RESULTS: Among 141 eligible patients, CA 19-9 declined during NT in 116. Following NT, 84 of 141 (60%) patients underwent resection. For post-NT resection, the positive predictive value of a decline and the negative predictive value of an increase in CA 19-9 were 70% and 88%, respectively. The normalization of CA 19-9 (post-NT < 40 U/ml) was associated with longer median overall survival among both non-resected (15 months versus 11 months; $P = 0.022$) and resected (38 months versus 26 months; $P = 0.020$) patients. Factors independently associated with shorter overall survival were no resection [hazard ratio (HR) 3.86, $P < 0.001$] and failure to normalize CA 19-9 (HR 2.13, $P = 0.001$). CONCLUSIONS: The serum CA 19-9 level represents a dynamic preoperative marker of tumour biology and response to NT, and provides prognostic information in both non-resected and resected patients with borderline resectable pancreatic cancer.

[237]

TÍTULO / TITLE: - Endoscopic ultrasound-guided fine needle aspiration and biopsy using a 22-gauge needle with side fenestration in pancreatic cystic lesions.

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

REVISTA / JOURNAL: - Dig Liver Dis. 2013 Jul 31. pii: S1590-8658(13)00222-3. doi: 10.1016/j.dld.2013.06.008.

●● Enlace al texto completo (gratis o de pago) [1016/j.dld.2013.06.008](https://doi.org/10.1016/j.dld.2013.06.008)

AUTORES / AUTHORS: - Barresi L; Tarantino I; Traina M; Granata A; Curcio G; Azzopardi N; Baccarini P; Liotta R; Fornelli A; Maimone A; Jovine E; Cennamo V; Fabbri C

INSTITUCIÓN / INSTITUTION: - Gastroenterology and Endoscopy Unit, ISMETT, Palermo, Italy. Electronic address: lbarresi@ismett.edu.

RESUMEN / SUMMARY: - **BACKGROUND:** Cytologic diagnosis by endoscopic ultrasound-guided fine needle aspiration is associated with low sensitivity and adequacy. A newly designed endoscopic ultrasound-guided fine needle biopsy device, endowed with a side fenestration, is now available. **AIMS:** We carried out a study with the aim of evaluating the feasibility, safety, and diagnostic yield of the 22-gauge needle with side fenestration for endoscopic ultrasound fine needle aspiration and biopsy of pancreatic cystic lesions. **METHODS:** 58 patients with 60 pancreatic cystic lesions consecutively referred for endoscopic ultrasound guided-fine needle aspiration were enrolled in a prospective, dual centre study, and underwent fine needle aspiration and biopsy with the 22-gauge needle with side fenestration. **RESULTS:** Fine needle aspiration and biopsy was technically feasible in all cases. In 39/60 (65%) pancreatic cystic lesions, the specimens were adequate for cyto-histologic assessment. In lesions with solid components, and in malignant lesions, adequacy was 94.4% ($p=0.0149$) and 100% ($p=0.0069$), respectively. Samples were adequate for histologic evaluation in 18/39 (46.1%) cases. There were only 2 (3.3%) mild complications. **CONCLUSIONS:** Fine needle aspiration and biopsy with the 22-gauge needle with side fenestration is feasible, and superior to conventional endoscopic ultrasound-guided fine needle aspiration cytology from cystic fluid, particularly in pancreatic cystic lesions with solid component or malignancy, with a higher diagnostic yield and with no increase in complication rate.

[238]

TÍTULO / TITLE: - Pancreaticoduodenectomy combined with vascular resection and reconstruction for patients with locally advanced pancreatic cancer: a multicenter, retrospective analysis.

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

REVISTA / JOURNAL: - PLoS One. 2013 Aug 2;8(8):e70340. doi: 10.1371/journal.pone.0070340. Print 2013.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0070340](https://doi.org/10.1371/journal.pone.0070340)

AUTORES / AUTHORS: - Gong Y; Zhang L; He T; Ding J; Zhang H; Chen G; Zhang D; Wu Z; Chen Q; Fan H; Wang Q; Bie P; Wang H

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

RESUMEN / SUMMARY: - OBJECTIVE: The aim of this study was to present the therapeutic outcome of patients with locally advanced pancreatic cancer treated with pancreatoduodenectomy combined with vascular resection and reconstruction in addition to highlighting the mortality/morbidity and main prognostic factors associated with this treatment. MATERIALS AND METHODS: We retrospectively analyzed the clinical and pathological data of a total of 566 pancreatic cancer patients who were treated with PD from five teaching hospitals during the period of December 2006-December 2011. This study included 119 (21.0%) patients treated with PD combined with vascular resection and reconstruction. We performed a detailed statistical analysis of various factors, including postoperative complications, operative mortality, survival rate, operative time, pathological type, and lymph node metastasis. RESULTS: The median survival time of the 119 cases that received PD combined with vascular resection was 13.3 months, and the 1-, 2-, and 3-year survival rates were 30.3%, 14.1%, and 8.1%, respectively. The postoperative complication incidence was 23.5%, and the mortality rate was 6.7%. For the combined vascular resection group, complications occurred in 28 cases (23.5%). For the group without vascular resection, complications occurred in 37 cases (8.2%). There was significant difference between the two groups ($p = 0.001$). The degree of tumor differentiation and the occurrence of complications after surgery were independent prognostic factors that determined the patients' long-term survival. CONCLUSIONS: Compared with PD without vascular resection, PD combined with vascular resection and reconstruction increased the incidence of postoperative complications. However, PD combined with vascular resection and reconstruction could achieve the complete removal of tumors without significantly increasing the mortality rate, and the median survival time was higher than that of patients who underwent palliative treatment. In addition, the two independent factors affecting the postoperative survival time were the degree of tumor differentiation and the presence or absence of postoperative complications.

[239]

TÍTULO / TITLE: - Biomarkers screening between preoperative and postoperative patients in pancreatic cancer.

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

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(7):4161-5.

AUTORES / AUTHORS: - Li P; Yang J; Ma QY; Wu Z; Huang C; Li XQ; Wang Z

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shanxi, China E-mail : zheng.wang11@mail.xjtu.edu.cn, zheng.wang11@mail.xjtu.edu.cn.

RESUMEN / SUMMARY: - Objective: To investigate discriminating protein patterns and potential biomarkers in serum samples between pre/postoperative pancreatic cancer patients and healthy controls. Methods: 23 serum samples from PC patients (12 preoperative and 11 postoperative) and 76 from healthy controls were analyzed using

matrix-assisted laser desorption and ionization time-of-flight mass spectrometry (MALDI-TOF MS) technique combined with magnetic beads-based weak cation-exchange chromatography (MB-WCX). ClinProTools software selected several markers that made a distinction between pancreatic cancer patients and healthy controls. Results: 49 m/z distinctive peaks were found among the three groups, of which 33 significant peaks with a $P < 0.001$ were detected. Two proteins could distinguish the preoperative pancreatic cancer patients from the healthy controls. About 15 proteins may be potential biomarkers in assessment of pancreatic cancer resection. Conclusion: MB-MALDI-TOF-MS method could generate serum peptidome profiles of pancreatic cancer and provide a new approach to identify potential biomarkers for diagnosis and prognosis of this malignancy.

[240]

TÍTULO / TITLE: - Everolimus in the treatment of patients with advanced pancreatic neuroendocrine tumors: latest findings and interpretations.

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

REVISTA / JOURNAL: - Therap Adv Gastroenterol. 2013 Sep;6(5):412-9. doi: 10.1177/1756283X13496970.

●● Enlace al texto completo (gratis o de pago) [1177 1756283X13496970](#) [pii]

●● Enlace al texto completo (gratis o de pago) [1177/1756283X13496970](#)

AUTORES / AUTHORS: - Liu E; Marincola P; Oberg K

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

RESUMEN / SUMMARY: - Pancreatic neuroendocrine tumors (pNETs) are a heterogeneous group of neoplasms with various clinical presentations. More than half of patients present with so-called nonfunctioning tumors with no hormone-related symptoms, whereas other tumors produce symptoms like gastric problems, ulcers, hypoglycemia, skin rash and diarrhea related to hormone production. The traditional treatment for pNETs over the last three decades has been cytotoxic agents, mainly streptozotocin plus 5-fluorouracil or doxorubicin. Most recently two new compounds have been registered worldwide for the treatment of pNETs, the mammalian target of rapamycin (mTOR) inhibitor everolimus and the tyrosine kinase inhibitor sunitinib. This paper concentrates on the use of mTOR inhibitors and the mechanisms of action. The mTOR pathway is altered in a number of pNETs. Everolimus (RAD001) is an orally active rapamycin analog and mTOR inhibitor. It blocks activity of the mTOR pathway by binding with high affinity to the cytoplasmic protein FKBP-12. The efficacy of everolimus in pNETs has been demonstrated in two multicenter studies (RADIANT 1 and 3). The RADIANT 3 study was a randomized controlled study in pNETs of everolimus 10 mg/day versus placebo, showing an increased progression-free survival (11.7 months versus 4.6 months) and hazard ratio of 0.35 ($p < 0.001$). Current studies

indicate that there is strong evidence to support the antitumor effect of rapalogs in pNETs. However, significant tumor reduction is very rarely obtained, usually in less than 10% of treated patients. Therefore, these drugs may be more effective in combination with other anticancer agents, including chemotherapy, targeted therapies as well as peptide receptor radiotherapy.

[241]

TÍTULO / TITLE: - Analysis of serum exosomal microRNAs and clinicopathologic features of patients with pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - World J Surg Oncol. 2013 Sep 4;11(1):219.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1477-7819-11-219](#)

AUTORES / AUTHORS: - Que R; Ding G; Chen J; Cao L

RESUMEN / SUMMARY: - BACKGROUND: Altered expression of serum microRNAs (miRNAs) have been reported to correlate with carcinogenesis and progression of pancreatic adenocarcinoma (PC), but descriptions of serum exosomal miRNAs in PC are still lacking. This study was designed to evaluate serum exosomal miRNA levels in PC patients and to investigate their relationships with clinicopathologic features and prognosis. METHODS: Four miRNAs (miR-17-5p, miR-21, miR-155 and miR-196^a) related to PC were selected for examination in our research. Serum miRNA was examined by RT-PCR in a group of 49 patients, including 22 with PCs, 6 with benign pancreatic tumors, 7 with ampullary carcinomas, 6 with chronic pancreatitis and 8 healthy participants. The clinicopathologic data were also collected, and PC patients were classified according to the presence of metastasis, tumor differentiation and advanced stage. RESULTS: There were low expressions of exosomal miR-155 and miR-196^a in serum samples of PC patients when U-6 was used as a control. Serum exosomal miR-17-5p was higher in PC patients than in non-PC patients and healthy participants. High levels of miR-17-5p were significantly correlated with metastasis and advanced stage of PC. The serum exosomal miR-21 level in PC was higher than that in the normal and chronic pancreatitis groups, but was not significantly correlated with PC differentiation and tumor stage. CONCLUSIONS: There were high expressions of serum exosomal miR-17-5p and miR-21 in PC patients. Examination of serum exosomal microRNA is a useful serum biomarker for PC diagnosis other than serum-free microRNA. It is postulated that exosomal miR-17-5p participates in the progression of PC.

[242]

TÍTULO / TITLE: - Immune infiltrates as predictive markers of survival in pancreatic cancer patients.

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

REVISTA / JOURNAL: - Front Physiol. 2013;4:210. doi: 10.3389/fphys.2013.00210.

- Enlace al texto completo (gratis o de pago) [3389/fphys.2013.00210](https://doi.org/10.1186/1746-1596-8-146)

AUTORES / AUTHORS: - Protti MP; De Monte L

INSTITUCIÓN / INSTITUTION: - Tumor Immunology Unit, Transplantation and Infectious Diseases, San Raffaele Scientific Institute Milan, Italy ; Division of Immunology, Transplantation and Infectious Diseases, San Raffaele Scientific Institute Milan, Italy.

RESUMEN / SUMMARY: - Pancreatic cancer is a devastating disease with dismal prognosis. The tumor microenvironment is composed by multiple cell types, molecular factors, and extracellular matrix forming a strong desmoplastic reaction, which is a hallmark of the disease. A complex cross-talk between tumor cells and the stroma exists with reciprocal influence that dictates tumor progression and ultimately the clinical outcome. In this context, tumor infiltrating immune cells through secretion of chemokine and cytokines exert an important regulatory role. Here we review the correlation between the immune infiltrates, evaluated on tumor samples of pancreatic cancer patients underwent surgical resection, and disease free and/or overall survival after surgery. Specifically, we focus on tumor infiltrating lymphocytes (TILs), mast cells (MCs) and macrophages that all contribute to a Th2-type inflammatory and immunosuppressive microenvironment. In these patients tumor immune infiltrates not only do not contribute to disease eradication but rather the features of Th2-type inflammation and immunosuppression is significantly associated with more rapid disease progression and reduced survival.

[243]

TÍTULO / TITLE: - Expression of CD44v6 and integrin-ss1 for the prognosis evaluation of pancreatic cancer patients after cryosurgery.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](https://doi.org/10.1186/1746-1596-8-146)

REVISTA / JOURNAL: - Diagn Pathol. 2013 Sep 2;8(1):146.

- Enlace al texto completo (gratis o de pago) [1186/1746-1596-8-146](https://doi.org/10.1186/1746-1596-8-146)

AUTORES / AUTHORS: - Chiu D; Zhou G; Qin D; Niu L; Cai J; He L; Tan D; Kecheng X

RESUMEN / SUMMARY: - BACKGROUND: Many previous studies demonstrated that cell adhesion molecules CD44v6 and integrin-ss1 had been extensively investigated as potential prognostic markers of various cancers. However, data in PC are scarce. METHODS: We now investigate CD44v6 and integrin-ss1 mRNA expression in PBMC by a triplex real-time RT-PCR assay and protein expression in plasma by ELISA. All specimens were collected from 54 PC patients who received the treatment of cryosurgery as well as 20 healthy individuals (control). RESULTS: The mRNA and protein expression levels of CD44v6 and integrin-ss1 in patients were significantly increased compared with control group ($P < 0.05$). The high CD44v6 mRNA and protein expression were significantly correlated with clinical stage, tumor differentiation, LNM, liver metastasis and decreased median DFS ($P < 0.05$), while the high integrin-ss1 mRNA and protein expression were significantly correlated with clinical stage, LNM, liver metastasis and decreased median DFS ($P < 0.05$). Clinical stage, LNM, liver metastasis,

CD44v6 mRNA and protein expression were the independent predictors of survival in PC patients ($P < 0.05$). Moreover, CD44v6 and integrin-ss1 mRNA and protein expression levels were significantly decreased in patients in 3 months after cryosurgery ($P < 0.05$). No significant difference was found in CD44v6 mRNA and protein expression between patients in 3 months after cryosurgery and control group ($P > 0.05$). CONCLUSION: CD44v6 and integrin-ss1 mRNA and protein expression in blood may serve as biomarkers for the development and metastasis of PC, and as prognostic indicators for PC. They may become useful predictors in assessing outcome of PC patients after cryosurgery. Virtual slides The virtual slides for this article can be found here: diagnosticpathology.diagnomx.eu/vs/4035308681009006.

[244]

TÍTULO / TITLE: - Concomitant targeting of multiple key transcription factors effectively disrupts cancer stem cells enriched in side population of human pancreatic cancer cells.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 11;8(9):e73942. doi: 10.1371/journal.pone.0073942.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0073942

AUTORES / AUTHORS: - Wang X; Liu Q; Hou B; Zhang W; Yan M; Jia H; Li H; Yan D; Zheng F; Ding W; Yi C; Hai Wang

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, Cancer Affiliated Hospital of Xinjiang Medical University, Urumqi, China.

RESUMEN / SUMMARY: - BACKGROUND: A major challenge in the treatment of pancreatic ductal adenocarcinoma is the failure of chemotherapy, which is likely due to the presence of the cancer stem cells (CSCs). OBJECTIVE: To identify side population (SP) cells and characterize s-like properties in human pancreatic cancer cell lines (h-PCCLs) and to exploit the efficacy of concomitant targeting of multiple key transcription factors governing the stemness of pancreatic CSCs in suppressing CSC-like phenotypes. METHODS: Flow cytometry and Hoechst 33342 DNA-binding dye efflux assay were used to sort SP and non-SP (NSP) cells from three h-PCCLs: PANC-1, SW1990, and BxPc-3. The self-renewal ability, invasiveness, migration and drug resistance of SP cells were evaluated. Expression of CSC marker genes was analyzed. Tumorigenicity was assessed using a xenograft model in nude mice. Effects of a complex decoy oligonucleotide (cdODN-SCO) designed to simultaneously targeting Sox2, Oct4 and c-Myc were assessed. RESULTS: CSCs were enriched in the side proportion (SP) cells contained in the h-PCCLs and they possessed aggressive growth, invasion, migration and drug-resistance properties, compared with NSP cells. SP cells overexpressed stem cell markers CD133 and ALDH1, pluripotency maintaining factors Nanog, Sox2 and Oct4, oncogenic transcription factor c-Myc, signaling molecule Notch1, and drug resistant gene ABCG2. Moreover, SP cells consistently demonstrated

significantly greater tumorigenicity than NSP cells in xenograft model of nude mice. CdODN-SOC efficiently suppressed all CSC properties and phenotypes, and minimized the tumorigenic capability of the SP cells and the resistance to chemotherapy. By comparison, the negative control failed to do so. CONCLUSION: The findings indicate that targeting the key genes conferring the stemness of CSCs can efficiently eliminate CSC-like phenotypes, and thus may be considered a new approach for cancer therapy. Specifically, the present study establishes the combination of Sox2/Oct4/c-Myc targeting as a potential anti-pancreatic cancer agent worthy of further studies in preclinical settings.

[245]

TÍTULO / TITLE: - Changes in dietary intake, body weight, nutritional status, and metabolic rate in a pancreatic cancer patient.

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

REVISTA / JOURNAL: - Clin Nutr Res. 2013 Jul;2(2):154-8. doi: 10.7762/cnr.2013.2.2.154. Epub 2013 Jul 23.

●● Enlace al texto completo (gratis o de pago) [7762/cnr.2013.2.2.154](#)

AUTORES / AUTHORS: - Kim SY; Wie GA; Lee WJ; Park SJ; Woo SM

INSTITUCIÓN / INSTITUTION: - Department of Clinical Nutrition, National Cancer Center, Goyang 410-769, Korea.

RESUMEN / SUMMARY: - Pancreatic cancer patients often have a poor prognosis and suffer from nutritional problems. Malnutrition is characterized by weight loss and decreased dietary intake, and is common among pancreatic cancer patients. The objective of this report was to describe the changes in dietary intake, body weight, nutritional status, and metabolic rate on a continuum from the time of diagnosis until the end of life in a patient with pancreatic cancer. In summary, the patient's nutritional status gradually declined, accompanied by extreme weight loss and decreased dietary intake. Conversely, resting energy expenditure, measured by indirect calorimetry, increased from 24 kcal/kg/day to 35 kcal/kg/day. Nutritional management during cancer treatment is important but may be challenging in pancreatic cancer patients.

[246]

TÍTULO / TITLE: - An absolute risk model to identify individuals at elevated risk for pancreatic cancer in the general population.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 13;8(9):e72311. doi: 10.1371/journal.pone.0072311.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0072311](#)

AUTORES / AUTHORS: - Klein AP; Lindstrom S; Mendelsohn JB; Steplowski E; Arslan AA; Bueno-de-Mesquita HB; Fuchs CS; Gallinger S; Gross M; Helzlsouer K; Holly EA; Jacobs EJ; Lacroix A; Li D; Mandelsohn MT; Olson SH; Petersen GM; Risch HA; Stolzenberg-

Solomon RZ; Zheng W; Amundadottir L; Albanes D; Allen NE; Bamlet WR; Boutron-Ruault MC; Buring JE; Bracci PM; Canzian F; Clipp S; Cotterchio M; Duell EJ; Elena J; Gaziano JM; Giovannucci EL; Goggins M; Hallmans G; Hassan M; Hutchinson A; Hunter DJ; Kooperberg C; Kurtz RC; Liu S; Overvad K; Palli D; Patel AV; Rabe KG; Shu XO; Slimani N; Tobias GS; Trichopoulos D; Van Den Eeden SK; Vineis P; Virtamo J; Wactawski-Wende J; Wolpin BM; Yu H; Yu K; Zeleniuch-Jacquotte A; Chanock SJ; Hoover RN; Hartge P; Kraft P

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, Maryland, United States of America ; Department of Pathology, Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins School of Medicine, Baltimore, Maryland, United States of America ; Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States of America.

RESUMEN / SUMMARY: - **PURPOSE:** We developed an absolute risk model to identify individuals in the general population at elevated risk of pancreatic cancer. **PATIENTS AND METHODS:** Using data on 3,349 cases and 3,654 controls from the PanScan Consortium, we developed a relative risk model for men and women of European ancestry based on non-genetic and genetic risk factors for pancreatic cancer. We estimated absolute risks based on these relative risks and population incidence rates. **RESULTS:** Our risk model included current smoking (multivariable adjusted odds ratio (OR) and 95% confidence interval: 2.20 [1.84-2.62]), heavy alcohol use (>3 drinks/day) (OR: 1.45 [1.19-1.76]), obesity (body mass index >30 kg/m²) (OR: 1.26 [1.09-1.45]), diabetes >3 years (nested case-control OR: 1.57 [1.13-2.18], case-control OR: 1.80 [1.40-2.32]), family history of pancreatic cancer (OR: 1.60 [1.20-2.12]), non-O ABO genotype (AO vs. OO genotype) (OR: 1.23 [1.10-1.37]) to (BB vs. OO genotype) (OR 1.58 [0.97-2.59]), rs3790844(chr1q32.1) (OR: 1.29 [1.19-1.40]), rs401681(5p15.33) (OR: 1.18 [1.10-1.26]) and rs9543325(13q22.1) (OR: 1.27 [1.18-1.36]). The areas under the ROC curve for risk models including only non-genetic factors, only genetic factors, and both non-genetic and genetic factors were 58%, 57% and 61%, respectively. We estimate that fewer than 3/1,000 U.S. non-Hispanic whites have more than a 5% predicted lifetime absolute risk. **CONCLUSION:** Although absolute risk modeling using established risk factors may help to identify a group of individuals at higher than average risk of pancreatic cancer, the immediate clinical utility of our model is limited. However, a risk model can increase awareness of the various risk factors for pancreatic cancer, including modifiable behaviors.

[247]

TÍTULO / TITLE: - Flavonoid apigenin modified gene expression associated with inflammation and cancer and induced apoptosis in human pancreatic cancer cells through inhibition of GSK-3beta/NF-kappaB signaling cascade.

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

REVISTA / JOURNAL: - Mol Nutr Food Res. 2013 Aug 14. doi: 10.1002/mnfr.201300307.

●● Enlace al texto completo (gratis o de pago) [1002/mnfr.201300307](https://doi.org/10.1002/mnfr.201300307)

AUTORES / AUTHORS: - Johnson JL; de Mejia EG

INSTITUCIÓN / INSTITUTION: - Division of Nutritional Sciences, University of Illinois at Urbana-Champaign, IL, USA.

RESUMEN / SUMMARY: - SCOPE: The objective was to examine the inhibitory effects of citrus fruit bioactive compounds on BxPC-3 and PANC-1 human pancreatic cancer cells, focusing on the antiproliferative mechanism of action of the flavonoid apigenin related to the glycogen synthase kinase-3beta/nuclear factor kappa B signaling pathway. METHODS AND RESULTS: Flavonoids, limonoids, phenolic acids, and ascorbic acid were tested for cytotoxic effects on BxPC-3 and PANC-1 cells; apigenin was the most potent (IC50 = 23 and 12 muM for 24 and 48 h for BxPC-3 and IC50 = 71 and 41 muM for 24 and 48 h for PANC-1). Apigenin induced pancreatic cell death through inhibition of the glycogen synthase kinase-3beta/nuclear factor kappa B signaling pathway. Apigenin arrested cell cycle at G2 /M phase (36 and 32% at 50 muM for BxPC-3 and PANC-1, respectively) with concomitant decrease in the expression of cyclin B1. Apigenin activated the mitochondrial pathway of apoptosis (44 and 14% at 50 muM for BxPC-3 and PANC-1, respectively) and modified the expression of apoptotic proteins. Apigenin highly upregulated the expression of cytokine genes IL17F (114.2-fold), LTA (33.1-fold), IL17C (23.2-fold), IL17A (11.3-fold), and IFNB1 (8.9-fold) in BxPC-3 cells, which potentially contributed to the anticancer properties. CONCLUSION: Flavonoids have a protective role in pancreatic cancer tumorigenesis.

[248]

TÍTULO / TITLE: - Adipose tissue-derived stem cells promote pancreatic cancer cell proliferation and invasion.

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

REVISTA / JOURNAL: - Braz J Med Biol Res. 2013 Sep;46(9):758-64. doi: 10.1590/1414-431X20132907. Epub 2013 Sep 27.

●● Enlace al texto completo (gratis o de pago) [1590/1414-431X20132907](https://doi.org/10.1590/1414-431X20132907)

AUTORES / AUTHORS: - Ji SQ; Cao J; Zhang QY; Li YY; Yan YQ; Yu FX

INSTITUCIÓN / INSTITUTION: - Second Military Medical University, Department of Liver Surgery I, Eastern Hepatobiliary Surgery Hospital, Shanghai, China.

RESUMEN / SUMMARY: - To explore the effects of adipose tissue-derived stem cells (ADSCs) on the proliferation and invasion of pancreatic cancer cells in vitro and the possible mechanism involved, ADSCs were cocultured with pancreatic cancer cells, and a cell counting kit (CCK-8) was used to detect the proliferation of pancreatic cancer cells. ELISA was used to determine the concentration of stromal cell-derived factor-1 (SDF-1) in the supernatants. RT-PCR was performed to detect the expression of the chemokine receptor CXCR4 in pancreatic cancer cells and ADSCs. An in vitro invasion assay was used to measure invasion of pancreatic cancer cells. SDF-1 was detected in

the supernatants of ADSCs, but not in pancreatic cancer cells. Higher CXCR4 mRNA levels were detected in the pancreatic cancer cell lines compared with ADSCs (109.3+/-10.7 and 97.6+/-7.6 vs 18.3+/-1.7, respectively; P<0.01). In addition, conditioned medium from ADSCs promoted the proliferation and invasion of pancreatic cancer cells, and AMD3100, a CXCR4 antagonist, significantly downregulated these growth-promoting effects. We conclude that ADSCs can promote the proliferation and invasion of pancreatic cancer cells, which may involve the SDF-1/CXCR4 axis.

[249]

TÍTULO / TITLE: - Contribution of FKBP5 genetic variation to gemcitabine treatment and survival in pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - PLoS One. 2013 Aug 1;8(8):e70216. doi: 10.1371/journal.pone.0070216. Print 2013.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0070216](https://doi.org/10.1371/journal.pone.0070216)

AUTORES / AUTHORS: - Ellsworth KA; Eckloff BW; Li L; Moon I; Fridley BL; Jenkins GD; Carlson E; Brisbin A; Abo R; Bamlet W; Petersen G; Wieben ED; Wang L

INSTITUCIÓN / INSTITUTION: - Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic, Rochester, Minnesota, USA.

RESUMEN / SUMMARY: - PURPOSE: FKBP51, (FKBP5), is a negative regulator of Akt. Variability in FKBP5 expression level is a major factor contributing to variation in response to chemotherapeutic agents including gemcitabine, a first line treatment for pancreatic cancer. Genetic variation in FKBP5 could influence its function and, ultimately, treatment response of pancreatic cancer. EXPERIMENTAL DESIGN: We set out to comprehensively study the role of genetic variation in FKBP5 identified by Next Generation DNA resequencing on response to gemcitabine treatment of pancreatic cancer by utilizing both tumor and germline DNA samples from 43 pancreatic cancer patients, including 19 paired normal-tumor samples. Next, genotype-phenotype association studies were performed with overall survival as well as with FKBP5 gene expression in tumor using the same samples in which resequencing had been performed, followed by functional genomics studies. RESULTS: In-depth resequencing identified 404 FKBP5 single nucleotide polymorphisms (SNPs) in normal and tumor DNA. SNPs with the strongest associations with survival or FKBP5 expression were subjected to functional genomic study. Electromobility shift assay showed that the rs73748206 "A(T)" SNP altered DNA-protein binding patterns, consistent with significantly increased reporter gene activity, possibly through its increased binding to Glucocorticoid Receptor (GR). The effect of rs73748206 was confirmed on the basis of its association with FKBP5 expression by affecting the binding to GR in lymphoblastoid cell lines derived from the same patients for whom DNA was used for resequencing.

CONCLUSION: This comprehensive FKBP5 resequencing study provides insights into the role of genetic variation in variation of gemcitabine response.

[250]

TÍTULO / TITLE: - Metabolic system alterations in pancreatic cancer patient serum: potential for early detection.

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

REVISTA / JOURNAL: - BMC Cancer. 2013 Sep 12;13(1):416.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-416](#)

AUTORES / AUTHORS: - Ritchie SA; Akita H; Takemasa I; Eguchi H; Pastural E; Nagano H; Monden M; Doki Y; Mori M; Jin W; Sajobi TT; Jayasinghe D; Chitou B; Yamazaki Y; White T; Goodenowe DB

RESUMEN / SUMMARY: - BACKGROUND: The prognosis of pancreatic cancer (PC) is one of the poorest among all cancers, due largely to the lack of methods for screening and early detection. New biomarkers for identifying high-risk or early-stage subjects could significantly impact PC mortality. The goal of this study was to find metabolic biomarkers associated with PC by using a comprehensive metabolomics technology to compare serum profiles of PC patients to healthy control subjects. METHODS: A non-targeted metabolomics approach based on high-resolution, flow-injection Fourier transform ion cyclotron resonance mass spectrometry (FI-FTICR-MS) was used to generate comprehensive metabolomic profiles containing 2478 accurate mass measurements from the serum of Japanese PC patients (n=40) and disease-free subjects (n=50). Targeted flow-injection tandem mass spectrometry (FI-MS/MS) assays for specific metabolic systems were developed and used to validate the FI-FTICR-MS results. A FI-MS/MS assay for the most discriminating metabolite discovered by FI-FTICR-MS (PC-594) was further validated in two USA Caucasian populations; one comprised 14 PCs, six intraductal papillary mucinous neoplasms (IPMN) and 40 controls, and a second comprised 1000 reference subjects aged 30 to 80, which was used to create a distribution of PC-594 levels among the general population. RESULTS: FI-FTICR-MS metabolomic analysis showed significant reductions in the serum levels of metabolites belonging to five systems in PC patients compared to controls (all $p < 0.000025$). The metabolic systems included 36-carbon ultra long-chain fatty acids, multiple choline-related systems including phosphatidylcholines, lysophosphatidylcholines and sphingomyelins, as well as vinyl ether-containing plasmalogen ethanolamines. ROC-AUCs based on FI-MS/MS of selected markers from each system ranged between 0.93 +/-0.03 and 0.97 +/-0.02. No significant correlations between any of the systems and disease-stage, gender, or treatment were observed. Biomarker PC-594 (an ultra long-chain fatty acid), was further validated using an independently-collected US Caucasian population (blinded analysis, n=60, $p=9.9E-14$, AUC=0.97 +/-0.02). PC-594 levels across 1000 reference subjects showed an inverse correlation with age, resulting in a drop in the AUC from 0.99 +/-0.01 to 0.90 +/-0.02

for subjects aged 30 to 80, respectively. A PC-594 test positivity rate of 5.0% in low-risk reference subjects resulted in a PC sensitivity of 87% and a significant improvement in net clinical benefit based on decision curve analysis. CONCLUSIONS: The serum metabolome of PC patients is significantly altered. The utility of serum metabolite biomarkers, particularly PC-594, for identifying subjects with elevated risk of PC should be further investigated.

[251]

TÍTULO / TITLE: - Unusual Features in an Adult Pancreatic Hemangioma: CT and MRI Demonstration.

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

REVISTA / JOURNAL: - Korean J Radiol. 2013 Sep;14(5):781-5. doi: 10.3348/kjr.2013.14.5.781. Epub 2013 Aug 30.

●● Enlace al texto completo (gratis o de pago) [3348/kjr.2013.14.5.781](#)

AUTORES / AUTHORS: - Lu ZH; Wu M

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Changshu Hospital of Soochow University, Jiangsu 215500, China.

RESUMEN / SUMMARY: - Hemangiomas in the pancreas are very rare and only a few cases in adulthood have been reported in the literature. We describe a case of pancreatic hemangiomas in an adult with unique imaging findings. A 23-year-old woman visited the hospital for an incidentally detected pancreatic mass. CT and MRI revealed a multilocular cyst with fluid-fluid levels and no obvious enhancement. The patient underwent surgery and the mass was confirmed as a pancreatic hemangioma. The radiological features and differential diagnosis of this rare lesion are discussed.

[252]

TÍTULO / TITLE: - Constitutive Activation of Rac1 in Pancreatic beta Cells Facilitates F-Actin Depolymerization but Exerts No Influence on the Increase of Pancreatic beta Cell Mass and Facilitation of Insulin Secretion.

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

REVISTA / JOURNAL: - Kobe J Med Sci. 2013 May 8;59(3):E72-80.

AUTORES / AUTHORS: - Shibutani Y; Asahara S; Teruyama K; Inoue H; Matsuda T; Seino S; Kido Y

INSTITUCIÓN / INSTITUTION: - Division of Diabetes and Endocrinology, Department of Internal Medicine, Kobe University Graduate School of Medicine, Kobe, Japan.

RESUMEN / SUMMARY: - Insulin secretion from pancreatic beta cells has an important role in the onset of type 2 diabetes. Insulin secretion from pancreatic beta cells is regulated by pancreatic beta cell mass and their insulin secretory function. By using pancreatic beta cell-specific Rac1-knockout mice, we recently showed that Rac1 deletion, even with no reduction in pancreatic beta cell mass, inhibits F-actin

depolymerization, which causes insulin secretion to decline. However, the effect of Rac1 deficiency on the growth and apoptosis of pancreatic beta cells was not clarified. Further, the effect of constitutive Rac1 activation on the secretion of insulin from pancreatic beta cells has not been studied. Here, we used pancreatic islets isolated from pancreatic beta cell-specific Rac1-knockout mice to evaluate the growth and apoptosis of pancreatic beta cells. We found that Rac1 deficiency does not influence the growth or apoptosis of pancreatic beta cells. Further, when a constitutively activated form of Rac1 (G12V) is expressed, F-actin depolymerization was increased in the pancreatic beta cell lines, which had no effect on pancreatic beta cell growth or glucose-stimulated insulin secretion. These findings indicate that excessive Rac1 expression or activation in pancreatic beta cells facilitates F-actin depolymerization, but has no effect on insulin secretion.

[253]

TÍTULO / TITLE: - The effect of simvastatin on lipid droplets accumulation in human embryonic kidney cells and pancreatic cancer cells.

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

REVISTA / JOURNAL: - Lipids Health Dis. 2013 Aug 21;12(1):126.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1476-511X-12-126](#)

AUTORES / AUTHORS: - Gbelcova H; Veda M; Laubertova L; Varga I; Vitek L; Kola M; Strnad H; Zelenka J; Bohmer D; Ruml T

RESUMEN / SUMMARY: - BACKGROUND: Statins (HMG-CoA reductase inhibitors) represent a major class of compounds for the treatment of hypercholesterolemia due to their ability to inhibit de novo cholesterol synthesis. In addition to their hypolipidemic effects, chemoprotective properties have been attributed to statins as well. These effects involve multiple mechanisms, which, however, are not known in detail. The aim of our study was to assess in non-malignant as well as cancer cells the impact of simvastatin on the amount of cytosolic lipid droplets (LDs) implicated in many biological processes including proliferation, inflammation, carcinogenesis, apoptosis, necrosis or growth arrest. METHODS: Human embryonic kidney cells HEK-293T and human pancreatic cancer cells MiaPaCa-2 were treated with simvastatin (6 and 12 μ M) for 24 and 48 hours respectively. Neutral lipid probe Nile Red was used for detection of LDs by fluorescence microscopy. Cellular cholesterol content was determined by HPLC. Changes in expression of genes related to lipid metabolism in simvastatin-treated MiaPaCa-2 cells were examined by DNA microarray analysis. Validation of gene expression changes was performed using quantitative RT-PCR. RESULTS: The treatment of the cells with simvastatin increased their intracellular content of LDs in both non-malignant as well as cancer cells, partially due to the uptake of cholesterol and triacylglycerols from medium; but in particular, due to enhanced synthesis of triacylglycerols as proved by significant overexpression of

genes related to de novo synthesis of triacylglyceroles and phospholipids. In addition, simvastatin also markedly influenced expression of genes directly affecting cell proliferation and signaling. CONCLUSIONS: Simvastatin treatment led to accumulation of cytosolic LDs within the examined cells, a phenomenon which might contribute to the antiproliferative effects of statins.

[254]

TÍTULO / TITLE: - 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 Aug 21. pii: S1931-5244(13)00249-1. doi: 10.1016/j.trsl.2013.06.009.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.trsl.2013.06.009](#)

AUTORES / AUTHORS: - Thaler J; Koder S; Kornek G; Pabinger I; Ay C

INSTITUCIÓN / INSTITUTION: - Clinical Division of Haematology and Haemostaseology, Department of Medicine I, Vienna, Austria; Comprehensive Cancer Center Vienna, Medical University of Vienna, Vienna General Hospital, Vienna, Austria.

RESUMEN / SUMMARY: - Highly elevated microparticle (MP)-associated tissue factor (TF) activity was found in patients with pancreatic cancer, one of the most prothrombotic malignancies. It remains to be elucidated whether MP-TF activity reflects the prothrombotic state in these patients. MP-TF activity levels and the TF-dependent and -independent effect of MPs on fibrin clot formation were determined in patients with metastatic pancreatic cancer (n = 27), in healthy individuals (n = 10) and in plasma samples from lipopolysaccharide (LPS)-stimulated blood (LPS-plasma), which is rich in monocyte-derived TF-bearing MPs. The median MP-TF activity was 1.06 pg/mL (range, from 0.19 to 10.34 pg/mL) in patients with pancreatic cancer, 0.61 pg/mL (range, from 0.36 to 0.79 pg/mL) in LPS-plasma, and 0.18 pg/mL (range, from 0.04 to 0.39 pg/mL) in healthy individuals. MPs derived from LPS-plasma had the strongest impact on fibrin clot formation time (median, 157.6 seconds; range, from 149.5 to 170.4 seconds). Fibrin clot formation occurred significantly later in MPs derived from patients with pancreatic cancer (median, 273.4 seconds; range, from 146.6 to 354.4 seconds; P < 0.001) and in healthy individuals (median, 299.0 seconds; range, from 261.1 to 417.9 seconds; P < 0.001). Only in MPs derived from LPS-plasma the fibrin clot formation time dependent strongly on TF (median prolongation after TF blockade: 68% in LPS-plasma, 10% in patients with pancreatic cancer, and 4% in healthy individuals). In conclusion, highly elevated MP-TF activity was found in patients with metastatic pancreatic cancer, but TF-bearing MPs had a small effect on fibrin clot formation. TF-bearing MPs might not be the main mediators of the prothrombotic state associated with pancreatic cancer. However, the small but significant increase in coagulation potential by TF-bearing MPs might contribute to the multifactorial pathogenesis of venous thromboembolism in pancreatic cancer.

[255]

TÍTULO / TITLE: - Gemcitabine-mediated tumour regression and p53-dependent gene expression: implications for colon and pancreatic cancer therapy.

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

REVISTA / JOURNAL: - Cell Death Dis. 2013 Sep 5;4:e791. doi: 10.1038/cddis.2013.307.

●● Enlace al texto completo (gratis o de pago) [1038/cddis.2013.307](#)

AUTORES / AUTHORS: - Hill R; Rabb M; Madureira PA; Gujar SA; Waisman DM; Giacomantonio CA; Lee PW

INSTITUCIÓN / INSTITUTION: - 1] Centre for Molecular and Structural Biomedicine, University of Algarve, Algarve, Portugal [2] Department of Microbiology & Immunology, Dalhousie University, Halifax, Nova Scotia, Canada [3] Department of Medicine, University of Algarve, Algarve, Portugal.

RESUMEN / SUMMARY: - Gemcitabine is a chemotherapeutic that is widely used for the treatment of a variety of haematological malignancies and has become the standard chemotherapy for the treatment of advanced pancreatic cancer. Combinational gemcitabine regimes (e.g.with doxorubicin) are being tested in clinical trials to treat a variety of cancers, including colon cancer. The limited success of these trials has prompted us to pursue a better understanding of gemcitabine's mechanism of cell killing, which could dramatically improve the therapeutic potential of this agent. For comparison, we included gamma irradiation that triggers robust cell cycle arrest and Cr(VI), which is a highly toxic chemical that induces a robust p53-dependent apoptotic response. Gemcitabine induced a potent p53-dependent apoptosis that correlated with the accumulation of pro-apoptotic proteins such as PUMA and Bax. This is accompanied by a drastic reduction in p21 and 14-3-3sigma protein levels, thereby significantly sensitizing the cells to apoptosis. In vitro and in vivo studies demonstrated that gemcitabine required PUMA transcription to instigate an apoptotic programme. This was in contrast to Cr(VI)-induced apoptosis that required Bax and was independent of transcription. An examination of clinical colon and pancreatic cancer tissues shows higher p53, p21, 14-3-3sigma and Bax expression compared with matched normal tissues, yet there is a near absence of PUMA protein. This may explain why gemcitabine shows only limited efficacy in the treatment of these cancers. Our results raise the possibility that targeting the Bax-dependent cell death pathway, rather than the PUMA pathway, could result in significantly improved patient outcome and prognosis for these cancers.

[256]

TÍTULO / TITLE: - Novel protein isoforms of carcinoembryonic antigen are secreted from pancreatic, gastric and colorectal cancer cells.

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

REVISTA / JOURNAL: - BMC Res Notes. 2013 Sep 26;6(1):381.

●● Enlace al texto completo (gratis o de pago) 1186/1756-0500-6-381

AUTORES / AUTHORS: - Hatakeyama K; Wakabayashi-Nakao K; Ohshima K; Sakura N; Yamaguchi K; Mochizuki T

RESUMEN / SUMMARY: - BACKGROUND: Carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5) is an oncofetal cell surface glycoprotein. Because of its high expression in cancer cells and secretion into serum, CEA has been widely used as a serum tumor marker. Although other members of CEACAM family were investigated for splice variants/variants-derived protein isoforms, few studies about the variants of CEACAM5 have been reported. In this study, we demonstrated the existence of novel CEACAM5 splice variants and splice variant-derived protein isoforms in gastrointestinal cancer cell lines. RESULTS: We identified two novel CEACAM5 splice variants in gastrointestinal (pancreatic, gastric, and colorectal) cancer cell lines. One of the variants possessed an alternative minor splice site that allowed generation of GC-AG intron. Furthermore, CEA protein isoforms derived from the novel splice variants were expressed in cancer cell lines and those protein isoforms were secreted into the culture medium. Although CEA protein isoforms always co-existed with the full-length protein, the secretion patterns of these isoforms did not correlate with the expression patterns. CONCLUSIONS: This is the first study to identify the expression of CEA isoforms derived from the novel splice variants processed on the unique splice site. In addition, we also revealed the secretion of those isoforms from gastrointestinal cancer cell lines. Our findings suggested that discrimination between the full-length and identified protein isoforms may improve the clinical utility of CEA as a tumor marker.

[257]

TÍTULO / TITLE: - Synchronous triple cancers of the pancreas, stomach, and cecum treated with s-1 followed by pancrelipase treatment of pancreatic exocrine insufficiency.

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

REVISTA / JOURNAL: - JOP. 2013 Sep 10;14(5):515-20. doi: 10.6092/1590-8577/1719.

AUTORES / AUTHORS: - Ohtsubo K; Ishikawa D; Nanjo S; Takeuchi S; Yamada T; Mouri H; Yamashita K; Yasumoto K; Gabata T; Matsui O; Ikeda H; Takamatsu Y; Iwakami S; Yano S

INSTITUCIÓN / INSTITUTION: - Division of Medical Oncology, Cancer Research Institute, Kanazawa University. Kanazawa, Japan. ohtsubo@staff.kanazawa-u.ac.jp.

RESUMEN / SUMMARY: - CONTEXT: Pancreatic cancer is frequently complicated by malignancies in other organs. However, synchronous triple cancers including pancreatic cancer have been seldom reported in the English language literature. CASE REPORT: We describe the rare case of a 77-year-old man with triple cancers of the pancreas, stomach, and cecum. Biopsies revealed that all three tumors were adenocarcinomas. The pancreatic and gastric tumors were positive for cytokeratin 7 and negative for cytokeratin 20, whereas the cecal tumor was negative for cytokeratin

7 and positive for cytokeratin 20. K-ras mutations were present at codon 12 in the pancreatic tumor and at codon 13 in the cecal tumor, but were absent from the gastric tumor. Since the three tumors had different characteristics, the patient was diagnosed with synchronous triple cancers. Because invasive surgery was required to remove all three tumors and the patient had risk factors for surgery, we elected to treat him with chemotherapy. All three cancers were markedly reduced in size by treatment with cycles of 100 mg/day S-1 for 2 weeks, followed by a 1-week rest. The patient later developed hypoproteinemia and anasarca, which was diagnosed as pancreatic exocrine insufficiency due to pancreatic head cancer. Treatment with pancrelipase resulted in dramatic improvements in hypoproteinemia and anasarca. CONCLUSIONS: This is the first case report in which S-1 was effective in triple cancers of the pancreas, stomach, and cecum. Patients with pancreatic head cancer should be monitored for pancreatic exocrine insufficiency.

[258]

TÍTULO / TITLE: - Cigarette smoking and pancreatic cancer risk: a revisit with an assessment of the nicotine dependence phenotype.

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

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(7):4409-13.

AUTORES / AUTHORS: - Nakao M; Hosono S; Ito H; Oze I; Watanabe M; Mizuno N; Yatabe Y; Yamao K; Niimi A; Tajima K; Tanaka H; Matsuo K

INSTITUCIÓN / INSTITUTION: - Division of Epidemiology and Prevention, Aichi Cancer Center Research Institute, Nagoya, Japan E-mail : kmatsuo@aichi-cc.jp.

RESUMEN / SUMMARY: - Background: Cigarette smoking is a well-established risk factor of pancreatic cancer (PC). Although an association between nicotine dependence phenotype, namely time to first cigarette (TTFC) after waking, and the risk of several smoking-related cancers has been reported, an association between TTFC and PC risk has not been reported. We assessed the impact of smoking behavior, particularly TTFC, on PC risk in a Japanese population. Materials and Methods: We conducted a case-control study using 341 PC and 1,705 non-cancer patients who visited Aichi Cancer Center in Nagoya, Japan. Exposure to risk factors, including smoking behavior, was assessed from the results of a self-administered questionnaire. The impact of smoking on PC risk was assessed with multivariate logistic regression analysis adjusted for potential confounders to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Results: Cigarettes per day (CPD) and/or smoking duration were significantly associated with PC risk, consistent with previous studies. For TTFC and PC risk, we found only a suggestive association: compared with a TTFC of more than 60 minutes, ORs were 1.15 (95%CI, 0.65- 2.04) for a TTFC of 30-60 minutes and 1.35 (95%CI, 0.85- 2.15) for that of 0-30 minutes (p trend=0.139). After adjustment for CPD or smoking duration, no association was observed between TTFC and PC. Conclusions: In this

study, we found no statistically significant association between TTFC and PC risk. Further studies concerning TTFC and PC risk are warranted.

[259]

TÍTULO / TITLE: - A Retrospective Study of Capecitabine/Temozolomide (CAPTEM) Regimen in the Treatment of Metastatic Pancreatic Neuroendocrine Tumors (pNETs) after Failing Previous Therapy.

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

REVISTA / JOURNAL: - JOP. 2013 Sep 10;14(5):498-501. doi: 10.6092/1590-8577/1589.

AUTORES / AUTHORS: - Saif MW; Kaley K; Brennan M; Garcon MC; Rodriguez G; Rodriguez T

INSTITUCIÓN / INSTITUTION: - Section of GI Cancers and Experimental Therapeutics, Tufts University School of Medicine. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - CONTEXT: Pancreatic neuroendocrine tumors (pNETs) are notoriously resistant to currently available chemotherapy agents. Preclinical data has suggested synergy between temozolomide and capecitabine. OBJECTIVE: To report a retrospective data on the efficacy and safety of capecitabine and temozolomide (CAPTEM regimen) in patients with metastatic pancreatic neuroendocrine tumors (pNETs) who have failed prior therapies. METHODS: We reviewed the medical records of 7 patients with metastatic pNETs who had had progressive cancer prior to treatment despite therapy, including long-acting release octreotide (60 mg/month), chemotherapy and hepatic chemoembolization. Capecitabine was administered at a flat dose of 1,000 mg orally twice daily on days 1-14 and temozolomide 200 mg/m² was given in two divided doses daily on days 10-14 of a 28-day cycle. Tumor assessments were repeated every two cycles and serum tumor markers were measured every cycle. Response to treatment was assessed using Response Evaluation Criteria in Solid Tumors (RECIST) parameters, and toxicity was graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0. RESULTS: Among 7 patients treated, three patients achieved a partial response, and two patients had stable disease. Total response rate was 43%, and clinical benefit (responders and stable disease) was 71%. Median duration of response was 8 months (range: 4-12 months). Grade 3 and 4 toxicities included grade 3 thrombocytopenia in one patient and grade 3 fatigue in one patient. The most common toxicities were grade 1 and 2 neutropenia, grade 1 fatigue, grade 1 and 2 hand-foot syndrome. CONCLUSIONS: Our retrospective study showed that modified CAPTEM regimen was well-tolerated and produced comparable response to historical data in neuroendocrine tumors, including pNETs. Our study is unique as it only included patients with pNETs. Further prospective studies are warranted to evaluate the combination of CAPTEM regimen with targeted therapies in pNETs.

[260]

TÍTULO / TITLE: - Clinicopathologic characteristics and surgical treatment of solid pseudopapillary tumor of the pancreas.

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

REVISTA / JOURNAL: - Hippokratia. 2013 Jan;17(1):68-72.

AUTORES / AUTHORS: - Huang Y; Feng JF

INSTITUCIÓN / INSTITUTION: - Nursing Department, Zhejiang Cancer Hospital, Hangzhou, China.

RESUMEN / SUMMARY: - Background and aim: Solid pseudopapillary tumor (SPT) of the pancreas is a very rare neoplasm of low malignant potential that mostly affects young women. The aim of the present study is to report our experience in surgical treatment of SPT and review of the literature. Material and methods: A retrospective review of three cases of SPT who were treated at our department during the last two years was performed. The clinicopathologic characteristics, surgical treatment, and prognosis are described in detail. Results: Case 1 described an asymptomatic SPT in a pregnant woman. To the best of our knowledge, only one case of SPT in pregnancy has been reported in the literature. Case 2 described an SPT in the pancreatic tail causing splenic infarction, and a distal pancreatectomy combined with splenectomy was performed. Case 3 described an SPT in the pancreatic head, for which a pancreatoduodenectomy was successfully performed. All of the three patients were followed up for 10-22 months without recurrence or metastases after the initial surgery at the time of reporting. Conclusions: At present, radical resection is the treatment of choice for SPT. Enucleation can be performed for tumors with complete amicula. Distal pancreatectomy combined with or without splenectomy can be performed for pancreatic body and/or tail tumor, and pancreatoduodenectomy for pancreatic head tumor. The prognosis of SPT is good.

[261]

TÍTULO / TITLE: - Cyclopamine increases the radiosensitivity of human pancreatic cancer cells by regulating the DNA repair signal pathway through an epidermal growth factor receptor-dependent pathway.

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

REVISTA / JOURNAL: - Mol Med Rep. 2013 Oct;8(4):979-83. doi: 10.3892/mmr.2013.1605. Epub 2013 Jul 30.

●● Enlace al texto completo (gratis o de pago) [3892/mmr.2013.1605](#)

AUTORES / AUTHORS: - Wu XY; Che J; Sun KK; Shen XJ; Yang D; Zhong N; Zhao H

INSTITUCIÓN / INSTITUTION: - Department of Gastrointestinal Surgery, Division of Thoracic Surgery, Kunshan First People's Hospital Affiliated to Jiangsu University, Kunshan, Jiangsu 215300, P.R. China.

RESUMEN / SUMMARY: - Pancreatic cancer is an aggressive malignancy with a characteristic metastatic course of disease and resistance to conventional

radiotherapy. As a result, the continual development of novel therapeutic agents is required to improve the current situation. In the present study, the effect of the hedgehog pathway inhibitor, cyclopamine, on cellular radiosensitivity was determined in KRASwt Colo357 and KRASmt SW1990 human pancreatic cancer cell lines using the clonogenic survival assay. Apoptosis and cell cycle distribution were detected using flow cytometry assay. Following irradiation (30 mins), residual doublestrand breaks were quantified by identification of gammaH2AX foci of micronuclei and radiationinduced gammaH2AX, pATM, DNAPKcs and Ku70 expression was analyzed using western blot analysis. The epidermal growth factor (EGF) and EGF receptor (EGFR) inhibitor, gefitinib, were utilized to determine the related mechanisms. The results revealed that cyclopamine treatment significantly reduced cell clonogenic survival but failed to induce apoptosis and radiationinduced G2 arrest. Flow cytometry revealed that cyclopamine treatment enhanced gammaH2AX foci in Colo357 and SW1990 cells exposed to irradiation. In addition, radiationinduced pATM, DNAPKcs and Ku70 were all inhibited. EGF also rescued pancreatic cancer cells from cyclopamineinduced H2AX phosphorylation following irradiation. Thus, cyclopamine enhanced the radiosensitivity of human pancreatic cancer cells, in part, through an EGFRdependent pathway, indicating a rational approach in combination with radiotherapy.

[262]

TÍTULO / TITLE: - Analysis of gene expression on ngn3 gene signaling pathway in endocrine pancreatic cancer.

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

REVISTA / JOURNAL: - Bioinformation. 2013 Aug 7;9(14):739-47. doi: 10.6026/97320630009739.

●● Enlace al texto completo (gratis o de pago) [6026/97320630009739](#)

AUTORES / AUTHORS: - Nagaraja P; Parashivamurthy K; Sidnal N; Mali S; Nagaraja D; Reddy S

INSTITUCIÓN / INSTITUTION: - Department of Bioinformatics, Scientific Bio-Minds, Bangalore-560092.

RESUMEN / SUMMARY: - In order to define the undifferentiated transcriptional factors present in neurogenesis of pancreatic beta-islet cells, we studied the effect of Pdx1 in embryonic stem cell derived endocrine lineage. There are undifferentiated transcriptional progenitors Pdx1+/Ptf1a+/Cpa1+ tracking the growth of acini, ducts, alpha and beta-islet cells. The upregulated transcriptional factors Pdx1 and ngn3 specify consequences of cell cycle regulation in early gut endocrine cells. The undifferentiated transcriptional factors basic helix loop helix (bHLH) protein regulate Ptf1a+/Cpa1+ in acini, ducts and it also regulate ngn3 to decrease expression of insulin and other pancreas secretions. The Pdx1+ and other unknown gene mutations show abnormal growth of neurogenesis in endocrine lineages. Using microarray based gene

expression analysis to determine undifferential gene ontology in tissue specific gene regulation and disease progression that common in both metabolic and biological signaling pathways. The data expression profiles of ngn3 of wild- type pancreatic islet and islet derived tumor stem cells provide information on endocrine specific ngn3 genes. Therefore, 3755 genes were significantly regulated by Ngn3 induced pancreatic islet cell development. Moreover 317 upregulated and 175 downregulated, 757 genes deemed as undifferential expressions in endocrine cell. Furthermore to predict signaling pathways that associates with diabetes is highlighted.

[263]

TÍTULO / TITLE: - Four-arm PEG cross-linked hyaluronic acid hydrogels containing PEGylated apoptotic TRAIL protein for treating pancreatic cancer.

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

REVISTA / JOURNAL: - Acta Biomater. 2013 Sep 8. pii: S1742-7061(13)00438-8. doi: 10.1016/j.actbio.2013.08.046.

●● Enlace al texto completo (gratis o de pago) [1016/j.actbio.2013.08.046](#)

AUTORES / AUTHORS: - Byeon HJ; Choi SH; Choi JS; Kim I; Shin BS; Lee ES; Park ES; Lee KC; Youn YS

INSTITUCIÓN / INSTITUTION: - School of Pharmacy, Sungkyunkwan University, 300 Cheoncheon-dong, Jangan-gu, Suwon 440-746, Republic of Korea.

RESUMEN / SUMMARY: - Four-arm polyethylene glycol (PEG) cross-linked hyaluronic acid (HA) hydrogels containing PEGylated tumor necrosis factor-related apoptosis-inducing ligand (PEG-TRAIL) were fabricated, and their antitumor effects were evaluated in pancreatic cell (Mia Paca-2)-xenografted mice. HA was conjugated with 4-arm PEG10k-amine (a cross-linker) at ratios of 100:1 and 100:2 using 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride as a cross-linker, and TRAIL or PEG-TRAIL was incorporated into these HA hydrogels. HA hydrogels at a 100:1 ratio were prepared in good yields (>88%), were moderately stiff, and gradually released PEG-TRAIL over approximately 14 days in vitro and over approximately 7 days in vivo (as determined by high-pressure liquid chromatography and infrared imaging). The released PEG-TRAIL was found to have obvious apoptotic activity in Mia Paca-2 cells. PEG-TRAIL HA hydrogels displayed remarkably more antitumor efficacy than TRAIL HA hydrogels in Mia Paca-2 cell-xenografted mice in terms of tumor volumes (size) and weights (453.2mm³ and 1.03g vs. 867.5mm³ and 1.86g). Furthermore, this improved antitumor efficacy was found to be due to the apoptotic activity of PEG-TRAIL in vivo (determined by a TUNEL assay) despite its substantially lower cytotoxicity than native TRAIL (IC₅₀ values: 71.8 and 202.5ngml⁻¹, respectively). This overall enhanced antitumor effect of PEG-TRAIL HA hydrogels appeared to be due to the increased stability of PEGylated TRAIL in HA hydrogels. These findings indicate that this HA hydrogel system combined with PEG-TRAIL should be considered a potential candidate for the treatment of pancreatic cancer.

[264]

TÍTULO / TITLE: - Prolonged clinical benefit of everolimus therapy in the management of high-grade pancreatic neuroendocrine carcinoma.

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

REVISTA / JOURNAL: - Case Rep Oncol. 2013 Aug 24;6(2):441-9. doi: 10.1159/000354754.

●● Enlace al texto completo (gratis o de pago) [1159/000354754](#)

AUTORES / AUTHORS: - Fonseca PJ; Uriol E; Galvan JA; Alvarez C; Perez Q; Villanueva N; Berros JP; Izquierdo M; Vieitez JM

INSTITUCIÓN / INSTITUTION: - Medical Oncology Department, Hospital Universitario Central de Asturias, Oviedo, España.

RESUMEN / SUMMARY: - Treatment options for patients with high-grade pancreatic neuroendocrine tumors (pNET) are limited, especially for those with progressive disease and for those who experience treatment failure. Everolimus, an oral inhibitor of mammalian target of rapamycin (mTOR), has been approved for the treatment of patients with low- or intermediate-grade advanced pNET. In the randomized phase III RADIANT-3 study in patients with low- or intermediate-grade advanced pNET, everolimus significantly increased progression-free survival (PFS) and decreased the relative risk for disease progression by 65% over placebo. This case report describes a heavily pretreated patient with high-grade pNET and liver and peritoneal metastases who achieved prolonged PFS, clinically relevant partial radiologic tumor response, and resolution of constitutional symptoms with improvement in Karnofsky performance status while receiving a combination of everolimus and octreotide long-acting repeatable (LAR). Radiologic and clinical responses were maintained for 19 months, with minimal toxicity over the course of treatment. This case supports the findings that the combination of everolimus plus octreotide LAR may be considered for use in patients with high-grade pNET and progressive disease. Although behavior and aggressiveness are different between low- or intermediate-grade and high-grade pNET, some high-grade pNET may express mTOR; hence, everolimus should be considered in a clinical trial.

[265]

TÍTULO / TITLE: - Antifreeze Protein Prolongs the Life-Time of Insulinoma Cells during Hypothermic Preservation.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 17;8(9):e73643. doi: 10.1371/journal.pone.0073643.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0073643](#)

AUTORES / AUTHORS: - Kamijima T; Sakashita M; Miura A; Nishimiya Y; Tsuda S

INSTITUCIÓN / INSTITUTION: - Bioproduction Research Institute, National Institute of Advanced Industrial Science and Technology (AIST), Sapporo, Hokkaido, Japan.

RESUMEN / SUMMARY: - It is sometimes desirable to preserve mammalian cells by hypothermia rather than freezing during short term transplantation. Here we found an ability of hypothermic (+4 degrees C) preservation of fish antifreeze protein (AFP) against rat insulinoma cells denoted as RIN-5F. The preservation ability was compared between type I-III AFPs and antifreeze glycoprotein (AFGP), which could be recently mass-prepared by a developed technique utilizing the muscle homogenates, but not the blood serum, of cold-adapted fishes. For AFGP, whose molecular weight is distributed in the range from 2.6 to 34 kDa, only the proteins less than 10 kDa were examined. The viability rate was evaluated by counting of the preserved RIN-5F cells unstained with trypan blue. Significantly, either AFPI or AFPIII dissolved into Euro-Collins (EC) solution at a concentration of 10 mg/ml could preserve approximately 60% of the cells for 5 days at +4 degrees C. The 5-day preserved RIN-5F cells retained the ability to secrete insulin. Only 2% of the cells were, however, preserved for 5 days without AFP. Confocal photomicroscopy experiments further showed the significant binding ability of AFP to the cell surface. These results suggest that fish AFP enables 5-day quality storage of the insulinoma cells collected from a donor without freezing.

[266]

TÍTULO / TITLE: - Human pancreatic cancer contains a side population expressing cancer stem cell-associated and prognostic genes.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 17;8(9):e73968. doi: 10.1371/journal.pone.0073968.

●● Enlace al texto completo (gratis o de pago) 1371/journal.pone.0073968

AUTORES / AUTHORS: - Van den Broeck A; Vankelecom H; Van Delm W; Gremeaux L; Wouters J; Allemeersch J; Govaere O; Roskams T; Topal B

INSTITUCIÓN / INSTITUTION: - Department of Abdominal Surgery, University Hospitals Leuven, Leuven, Belgium ; Laboratory of Tissue Plasticity, Research Unit of Embryo and Stem Cells, Department of Development & Regeneration, University of Leuven (KU Leuven), Leuven, Belgium.

RESUMEN / SUMMARY: - In many types of cancers, a side population (SP) has been identified based on high efflux capacity, thereby enriching for chemoresistant cells as well as for candidate cancer stem cells (CSC). Here, we explored whether human pancreatic ductal adenocarcinoma (PDAC) contains a SP, and whether its gene expression profile is associated with chemoresistance, CSC and prognosis. After dispersion into single cells and incubation with Hoechst dye, we analyzed human PDAC resections specimens using flow cytometry (FACS). We identified a SP and main population (MP) in all human PDAC resection specimens (n = 52) analyzed, but detected immune (CD45(+)) and endothelial (CD31(+)) cells in this fraction together with tumor cells. The SP and MP cells, or more purified fractions depleted from CD31(+)/CD45(+) cells (pSP and pMP), were sorted by FACS and subjected to whole-

genome expression analysis. This revealed upregulation of genes associated with therapy resistance and of markers identified before in putative pancreatic CSC. pSP gene signatures of 32 or 10 up- or downregulated genes were developed and tested for discriminatory competence between pSP and pMP in different sets of PDAC samples. The prognostic value of the pSP genes was validated in a large independent series of PDAC patients (n = 78) using nCounter analysis of expression (in tumor versus surrounding pancreatic tissue) and Cox regression for disease-free and overall survival. Of these genes, expression levels of ABCB1 and CXCR4 were correlated with worse patient survival. Thus, our study for the first time demonstrates that human PDAC contains a SP. This tumor subpopulation may represent a valuable therapeutic target given its chemoresistance- and CSC-associated gene expression characteristics with potential prognostic value.

[267]

TÍTULO / TITLE: - In Vitro Evaluation of HEMA-Copolymers Targeted to HER2 Expressing Pancreatic Tumor Cells for Image Guided Drug Delivery.

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

REVISTA / JOURNAL: - Macromol Biosci. 2013 Aug 28. doi: 10.1002/mabi.201300167.

●● Enlace al texto completo (gratis o de pago) [1002/mabi.201300167](#)

AUTORES / AUTHORS: - Buckway B; Wang Y; Ray A; Ghandehari H

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutics and Pharmaceutical Chemistry, Utah Center for Nanomedicine, Nano Institute of Utah University of Utah, 36 S Wasatch Dr., SMBB 5515, Salt Lake City, UT, 84112, USA; Center for Nanomedicine, Nano Institute of Utah, University of Utah, Salt Lake City, UT, 84112, USA.

RESUMEN / SUMMARY: - Personalized medicine for the treatment of pancreatic cancer is one potential avenue which can prevent the dire outcome of this difficult to treat disease. Image guided drug delivery (IGDD) is a method allowing real-time imaging of drug therapy in order to predict the potential efficacy and safety of a given treatment. Water soluble macromolecular drug carriers such as N-(2-hydroxypropyl)methacrylamide (HPMA) copolymers provide multifunctional platforms for the construction of such IGDD systems. HPMA copolymer conjugates containing gemcitabine, a targeting ligand for HER2 receptors overexpressed in some pancreatic cancers, and an $^{111}\text{In}^{3+}$ chelating agent are synthesized, characterized, and evaluated in vitro for their potential use as an IGDD system for pancreatic tumors. The conjugates are capable of binding to pancreatic tumor cell lines which express HER2. In vitro drug release is achieved under physiological and acidic pH environments. The chelated radioisotopes are stable in the presence of mouse serum. The conjugates are effective in killing pancreatic tumor cell lines in vitro. These copolymers have potential for further preclinical evaluation in pancreatic tumor models.

[268]

TÍTULO / TITLE: - Oncosuppressive Suicide Gene Virotherapy "PVH1-γCD/5-FC" for Pancreatic Peritoneal Carcinomatosis Treatment: NFκappaB and Akt/PI3K Involvement.

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

REVISTA / JOURNAL: - PLoS One. 2013;8(8):e70594. doi: 10.1371/journal.pone.0070594.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0070594](https://doi.org/10.1371/journal.pone.0070594)

AUTORES / AUTHORS: - Rejiba S; Bigand C; Parmentier C; Masmoudi A; Hajri A

INSTITUCIÓN / INSTITUTION: - Biologie des tumeurs, Universite de Strasbourg, Strasbourg, France.

[269]

TÍTULO / TITLE: - Intestinal-type of differentiation predicts favourable overall survival: confirmatory clinicopathological analysis of 198 periampullary adenocarcinomas of pancreatic, biliary, ampullary and duodenal origin.

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

REVISTA / JOURNAL: - BMC Cancer. 2013 Sep 22;13(1):428.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-428](https://doi.org/10.1186/1471-2407-13-428)

AUTORES / AUTHORS: - Bronsert P; Kohler I; Werner M; Makowiec F; Kuesters S; Hoepfner J; Hopt UT; Keck T; Bausch D; Wellner UF

RESUMEN / SUMMARY: - BACKGROUND: Periampullary adenocarcinomas comprise pancreatic, distal bile duct, ampullary and duodenal adenocarcinoma. The epithelia of these anatomical structures share a common embryologic origin from the foregut. With steadily increasing numbers of pancreatoduodenectomies over the last decades, pathologists, surgeons and oncologists are more often confronted with the diagnosis of "other than pancreatic" periampullary cancers. The intestinal subtype of ampullary cancer has been shown to correlate with better prognosis. METHODS: Histological subtype and immunohistochemical staining pattern for CK7, CK20 and CDX2 were assessed for n = 198 cases of pancreatic ductal, distal bile duct, ampullary and duodenal adenocarcinoma with clinical follow-up. Routine pathological parameters were included in survival analysis performed with SPSS 20. RESULTS: In univariate analysis, intestinal subtype was associated with better survival in ampullary, pancreatic ductal and duodenal adenocarcinoma. The intestinal type of pancreatic ductal adenocarcinoma was not associated with intraductal papillary mucinous neoplasm and could not be reliably diagnosed by immunohistochemical staining pattern alone. Intestinal differentiation and lymph node ratio, but not tumor location were independent predictors of survival when all significant predictor variables from univariate analysis (grade, TNM stage, presence of precursor lesions, surgical margin status, perineural, vascular and lymphatic vessel invasion, CK7 and CDX2 staining pattern) were included in a Cox proportional hazards model. CONCLUSIONS: Intestinal type differentiation and lymph node ratio but not tumor location are independent prognostic factors in pooled analysis of periampullary adenocarcinomas. We conclude

that differentiation is more important than tumor location for prognostic stratification in periampullary adenocarcinomas.

[270]

TÍTULO / TITLE: - Pharmacological reversal of histone methylation presensitizes pancreatic cancer cells to nucleoside drugs: in vitro optimization and novel nanoparticle delivery studies.

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

REVISTA / JOURNAL: - PLoS One. 2013 Aug 6;8(8):e71196. doi: 10.1371/journal.pone.0071196. Print 2013.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0071196](https://doi.org/10.1371/journal.pone.0071196)

AUTORES / AUTHORS: - Hung SW; Mody H; Marrache S; Bhutia YD; Davis F; Cho JH; Zastre J; Dhar S; Chu CK; Govindarajan R

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical and Biomedical Sciences, The University of Georgia, Athens, Georgia, United States of America.

RESUMEN / SUMMARY: - We evaluated the potential of an investigational histone methylation reversal agent, 3-deazaneplanocin A (DZNep), in improving the chemosensitivity of pancreatic cancer to nucleoside analogs (i.e., gemcitabine). DZNep brought delayed but selective cytotoxicity to pancreatic cancer cells without affecting normal human pancreatic ductal epithelial (HPDE) cells. Co-exposure of DZNep and gemcitabine induced cytotoxic additivity or synergism in both well- and poorly-differentiated pancreatic cell lines by increased apoptosis. In contrast, DZNep exerted antagonism with gemcitabine against HPDE cells with significant reduction in cytotoxicity compared with the gemcitabine-alone regimen. DZNep marginally depended on purine nucleoside transporters for its cytotoxicity, but the transport dependence was circumvented by acyl derivatization. Drug exposure studies revealed that a short priming with DZNep followed by gemcitabine treatment rather than co-treatment of both agents to produce a maximal chemosensitization response in both gemcitabine-sensitive and gemcitabine-resistant pancreatic cancer cells. DZNep rapidly and reversibly decreased trimethylation of histone H3 lysine 27 but increased trimethylation of lysine 9 in an EZH2- and JMJD1A/2C-dependent manner, respectively. However, DZNep potentiation of nucleoside analog chemosensitization was found to be temporally coupled to trimethylation changes in lysine 27 and not lysine 9. Polymeric nanoparticles engineered to chronologically release DZNep followed by gemcitabine produced pronounced chemosensitization and dose-lowering effects. Together, our results identify that an optimized DZNep exposure can presensitize pancreatic cancer cells to anticancer nucleoside analogs through the reversal of histone methylation, emphasizing the promising clinical utilities of epigenetic reversal agents in future pancreatic cancer combination therapies.

[271]

TÍTULO / TITLE: - Endoscopic ultrasound-guided fine needle aspiration of solid pseudopapillary tumors of the pancreas: a report of three cases.

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

REVISTA / JOURNAL: - Korean J Intern Med. 2013 Sep;28(5):599-604. doi: 10.3904/kjim.2013.28.5.599. Epub 2013 Aug 14.

●● Enlace al texto completo (gratis o de pago) [3904/kjim.2013.28.5.599](#)

AUTORES / AUTHORS: - Park HY; Lee YJ; Lee JH; Lee MJ; Lee JK; Lee KT; Lee KH

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - The solid pseudopapillary tumor (SPT) of the pancreas is a rare but low-grade malignant tumor with a good prognosis after surgical excision. Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) is a minimally invasive, safe and reliable way of diagnosing SPT by providing characteristic cytological and immunochemical specimens. Definitive preoperative diagnosis leads to targeted and minimally invasive surgical resection. In this study, we report three cases of SPTs that were diagnosed through EUS-FNA and underwent successful laparoscopic surgery.

[272]

TÍTULO / TITLE: - Long-term survival after resection of pancreatic ductal adenocarcinoma with para-aortic lymph node metastasis: case report.

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

REVISTA / JOURNAL: - World J Surg Oncol. 2013 Aug 14;11(1):195. doi: 10.1186/1477-7819-11-195.

●● Enlace al texto completo (gratis o de pago) [1186/1477-7819-11-195](#)

AUTORES / AUTHORS: - Masui T; Kubota T; Aoki K; Miyamoto T; Nagata J; Morino K; Fukugaki A; Takamura M; Sugimoto S; Onuma H; Tokuka A

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Kyoto University, Kyoto, Japan. tmasui@kuhp.kyoto-u.ac.jp

RESUMEN / SUMMARY: - Pancreatic cancer patients with para-aortic lymph node metastasis have a poor prognosis and patients living longer than 3 years are rare. We had a patient with pancreatic cancer who survived for more than 10 years after removal of the para-aortic lymph node metastasis. A 57-year-old woman was diagnosed with pancreatic head cancer and underwent a pancreaticoduodenectomy with subtotal gastric resection following Whipple reconstruction in 2000. Para-aortic lymph node metastasis was detected during the operation by intraoperative pathological diagnosis and an extended lymphadenectomy was performed with vascular skeletonization of the celiac and superior mesenteric arteries. In 2004, a low-density area was detected around the superior mesenteric artery (SMA) 5 cm from its root and she was treated with gemcitabine, and the area was undetectable after 3 years of treatment. In 2010, computed tomography showed a low-density area around

the same lesion with an increased carcinoembryonic antigen level. After 4 months of gemcitabine treatment, we resected the tumor en bloc with the associated superior mesenteric vein and perineural tissue. Histopathological examination of the resected specimen revealed a well-differentiated tubular adenocarcinoma that closely resembled the original primary pancreatic cancer, indicating perineural recurrence 10 years after the initial resection. She had no recurrence around the SMA for more than one year. Although a meta-analysis has not proved the efficacy of preventive radical dissection, this case indicates that a patient with well-differentiated, chemotherapy-responsive pancreatic cancer with para-aortic lymph node metastasis could have a long survival time through extended dissection of the lymph nodes.

[273]

TÍTULO / TITLE: - Moringa Oleifera aqueous leaf extract down-regulates nuclear factor-kappaB and increases cytotoxic effect of chemotherapy in pancreatic cancer cells.

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

REVISTA / JOURNAL: - BMC Complement Altern Med. 2013 Aug 19;13:212. doi: 10.1186/1472-6882-13-212.

●● Enlace al texto completo (gratis o de pago) [1186/1472-6882-13-212](#)

AUTORES / AUTHORS: - Berkovich L; Earon G; Ron I; Rimmon A; Vexler A; Lev-Ari S

INSTITUCIÓN / INSTITUTION: - Laboratory of Herbal Medicine and Cancer Research, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel. Shaharl@tasmc.health.gov.il.

RESUMEN / SUMMARY: - BACKGROUND: Fewer than 6% patients with adenocarcinoma of the pancreas live up to five years after diagnosis. Chemotherapy is currently the standard treatment, however, these tumors often develop drug resistance over time. Agents for increasing the cytotoxic effects of chemotherapy or reducing the cancer cells' chemo-resistance to the drugs are required to improve treatment outcome. Nuclear factor kappa B (NF-kB), a pro-inflammatory transcription factor, reportedly plays a significant role in the resistance of pancreatic cancer cells to apoptosis-based chemotherapy. This study investigated the effect of aqueous Moringa Oleifera leaf extract on cultured human pancreatic cancer cells - Panc-1, p34, and COLO 357, and whether it can potentiate the effect of cisplatin chemotherapy on these cells.

METHODS: The effect of Moringa Oleifera leaf extract alone and in combination with cisplatin on the survival of cultured human pancreatic cancer cells was evaluated by XTT-based colorimetric assay. The distribution of Panc-1 cells in the cell cycle following treatment with Moringa leaf extract was evaluated by flow cytometry, and evaluations of protein levels were via immunoblotting. Data of cell survival following combined treatments were analyzed with CalcuSyn software. **RESULTS:** Moringa Oleifera leaf extract inhibited the growth of all pancreatic cell lines tested. This effect was significant in all cells following exposure to ≥ 0.75 mg/ml of the extract. Exposure of Panc-1 cells to Moringa leaf extract induced an elevation in the sub-G1 cell population of the cell-cycle, and reduced the expression of p65, p-IkB α and IkB α proteins

in crude cell extracts. Lastly, Moringa Oleifera leaf extract synergistically enhanced the cytotoxic effect of cisplatin on Panc-1 cells. CONCLUSION: Moringa Oleifera leaf extract inhibits the growth of pancreatic cancer cells, the cells NF-kappaB signaling pathway, and increases the efficacy of chemotherapy in human pancreatic cancer cells.

[274]

TÍTULO / TITLE: - Prediction of glycan motifs using quantitative analysis of multi-lectin binding: Motifs on MUC1 produced by cultured pancreatic cancer cells.

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

REVISTA / JOURNAL: - Proteomics Clin Appl. 2013 Aug 19. doi: 10.1002/prca.201300069.

●● Enlace al texto completo (gratis o de pago) [1002/prca.201300069](#)

AUTORES / AUTHORS: - McCarter C; Kletter D; Tang H; Partyka K; Ma Y; Singh S; Yadav J; Bern M; Haab BB

INSTITUCIÓN / INSTITUTION: - Van Andel Research Institute, Grand Rapids, MI, USA.

RESUMEN / SUMMARY: - PURPOSE: Lectins are valuable tools for detecting specific glycans in biological samples, but the interpretation of the measurements can be ambiguous due to the complexities of lectin specificities. Here, we present an approach to improve the accuracy of interpretation by converting lectin measurements into quantitative predictions of the presence of various glycan motifs. EXPERIMENTAL DESIGN: The conversion relies on a database of analyzed glycan array data that provides information on the specificities of the lectins for each of the motifs. We tested the method using measurements of lectin binding to glycans on glycan arrays and then applied the method to predicting motifs on the protein mucin 1 (MUC1) expressed in eight different pancreatic cancer cell lines. RESULTS: The combined measurements from several lectins were more accurate than individual measurements for predicting the presence or absence of motifs on arrayed glycans. The analysis of MUC1 revealed that each cell line expressed a unique pattern of glycoforms, and that the glycoforms significantly differed between MUC1 collected from conditioned media and MUC1 collected from cell lysates. CONCLUSIONS AND CLINICAL RELEVANCE: This new method could provide more accurate analyses of glycans in biological sample and make the use of lectins more practical and effective for a broad range of researchers.

[275]

TÍTULO / TITLE: - Comparison of efficacy of Salmonella typhimurium A1-R and chemotherapy on stem-like and non-stem human pancreatic cancer cells.

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

REVISTA / JOURNAL: - Cell Cycle. 2013 Sep 1;12(17):2774-80. doi: 10.4161/cc.25872. Epub 2013 Aug 6.

●● Enlace al texto completo (gratis o de pago) [4161/cc.25872](#)

AUTORES / AUTHORS: - Hiroshima Y; Zhao M; Zhang Y; Maawy A; Hassanein MK; Uehara F; Miwa S; Yano S; Momiyama M; Suetsugu A; Chishima T; Tanaka K; Bouvet M; Endo I; Hoffman RM

INSTITUCIÓN / INSTITUTION: - AntiCancer, Inc; San Diego, CA USA; Department of Surgery; University of California San Diego; San Diego, CA USA; Yokohama City University Graduate School of Medicine; Yokohama, Japan.

RESUMEN / SUMMARY: - The XPA1 human pancreatic cancer cell line is dimorphic, with spindle stem-like cells and round non-stem cells. We report here the in vitro IC 50 values of stem-like and non-stem XPA1 human pancreatic cells for: (1) 5-fluorouracil (5-FU), (2) cisplatinum (CDDP), (3) gemcitabine (GEM), and (4) tumor-targeting Salmonella typhimurium A1-R (A1-R). IC 50 values of stem-like XPA1 cells were significantly higher than those of non-stem XPA1 cells for 5-FU (P = 0.007) and CDDP (P = 0.012). In contrast, there was no difference between the efficacy of A1-R on stem-like and non-stem XPA1 cells. In vivo, 5-FU and A1-R significantly reduced the tumor weight of non-stem XPA1 cells (5-FU; P = 0.028; A1-R; P = 0.011). In contrast, only A1-R significantly reduced tumor weight of stem-like XPA1 cells (P = 0.012). The combination A1-R with 5-FU improved the antitumor efficacy compared with 5-FU monotherapy on the stem-like cells (P = 0.004). The results of the present report indicate A1-R is a promising therapy for chemo-resistant pancreatic cancer stem-like cells.

[276]

TÍTULO / TITLE: - A spheroid-based 3-D culture model for pancreatic cancer drug testing, using the acid phosphatase assay.

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

REVISTA / JOURNAL: - Braz J Med Biol Res. 2013 Aug;46(7):634-42. doi: 10.1590/1414-431X20132647. Epub 2013 Jul 22.

●● Enlace al texto completo (gratis o de pago) [1590/1414-431X20132647](#)

AUTORES / AUTHORS: - Wen Z; Liao Q; Hu Y; You L; Zhou L; Zhao Y

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

RESUMEN / SUMMARY: - Current therapy for pancreatic cancer is multimodal, involving surgery and chemotherapy. However, development of pancreatic cancer therapies requires a thorough evaluation of drug efficacy in vitro before animal testing and subsequent clinical trials. Compared to two-dimensional culture of cell monolayer, three-dimensional (3-D) models more closely mimic native tissues, since the tumor microenvironment established in 3-D models often plays a significant role in cancer progression and cellular responses to the drugs. Accumulating evidence has highlighted the benefits of 3-D in vitro models of various cancers. In the present study, we have developed a spheroid-based, 3-D culture of pancreatic cancer cell lines

MIAPaCa-2 and PANC-1 for pancreatic drug testing, using the acid phosphatase assay. Drug efficacy testing showed that spheroids had much higher drug resistance than monolayers. This model, which is characteristically reproducible and easy and offers rapid handling, is the preferred choice for filling the gap between monolayer cell cultures and in vivo models in the process of drug development and testing for pancreatic cancer.

[277]

TÍTULO / TITLE: - A case of elderly-onset type 1 diabetes mellitus: negative for antiglutamic acid dehydrogenase antibody and positive insulinoma-associated tyrosine phosphatase-like protein-2 antibody.

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

REVISTA / JOURNAL: - Nihon Ronen Igakkai Zasshi. 2013;50(3):404-8.

AUTORES / AUTHORS: - Chiba Y; Ynie J; Kimbara Y; Tamura Y; Mori S; Ito H; Araki A

INSTITUCIÓN / INSTITUTION: - Department of Endocrinology and Metabolism, Tokyo Metropolitan Geriatric Hospital.

RESUMEN / SUMMARY: - An 83-year-old Japanese woman given a diagnosis of type 2 diabetes mellitus 3 years previously was hospitalized for markedly elevated plasma glucose (386 mg/dl) and glycated hemoglobin (9.3%) levels. Laboratory study results showed urinary connecting peptide immunoreactivity (CPR) concentrations of 8.9 mug/day and serum CPR levels <0.2 ng/ml before and 0.3 ng/ml 6 min after glucagon administration, indicating decreased insulin secretion. Although antiglutamic acid dehydrogenase (GAD) antibody levels were negative, insulinoma-associated tyrosine phosphatase-like protein-2 (IA-2) antibody levels were positive (50 U/ml), leading to a diagnosis of type 1 diabetes mellitus. Furthermore, human leukocyte antigen (HLA) typing revealed DRB1(*)0901, a diabetes-susceptibility gene. Intensive insulin therapy was initiated. This was a rare case of elderly-onset type 1 diabetes.

[278]

TÍTULO / TITLE: - Efficacy of multi-detector computerized tomography scan, endoscopic ultrasound, and laparoscopy for predicting tumor resectability in pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Indian J Gastroenterol. 2013 Aug 28.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s12664-013-0353-y](#)

AUTORES / AUTHORS: - Baghbanian M; Salmanroghani H; Baghbanian A; Bakhtpour M; Shabazkhani B

INSTITUCIÓN / INSTITUTION: - Department Gastroenterology, Shaheed Sadoughi University of Medical Sciences, Yazd, Iran, baghbanian1352@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: Definitive treatment for pancreatic adenocarcinoma is surgical resection. Endoscopic ultrasound (EUS), multi-detector computerized tomography scan (MDCT), and laparoscopy are current preoperative methods for assessing the resectability in this malignancy. This study compared the efficacy of these methods in predicting the resectability of pancreatic adenocarcinoma. METHODOLOGY: One hundred and fifty-seven patients considered for resection of pancreatic adenocarcinoma in two centers in Iran were evaluated. All of the patients were evaluated by MDCT and/or EUS; ones that had resectable tumor in imaging were assessed by laparoscopy/laparotomy. Patients undergoing pancreaticoduodenectomy were followed for 2 years. RESULTS: The majority (67 %) were male. The mean age was 66 years. The lesion was situated in the head of pancreas in 127 cases (81 %). Tumor resectability rate according to the MDCT scan/EUS, laparoscopy, and laparotomy was 6 %, 5 %, and 3 %, respectively. Only 3 % of the pancreatic adenocarcinoma cases were resectable at the time of diagnosis. Fifty percent of patients predicted to have resectable tumor according to MDCT/EUS and 37.5 % of cases that had resectable disease in laparoscopy were found to have unresectable lesions at laparotomy and or postsurgical follow up. CONCLUSIONS: Prognosis continues to be dismal for pancreatic adenocarcinoma, and better methods to assess tumor resectability are needed.

[279]

TÍTULO / TITLE: - Pancreatic cancer mortality in Serbia from 1991-2010 - a joinpoint analysis.

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

REVISTA / JOURNAL: - Croat Med J. 2013 Aug 28;54(4):369-75.

AUTORES / AUTHORS: - Ilic M; Vlajinac H; Marinkovic J; Kocev N

INSTITUCIÓN / INSTITUTION: - Ilic Milena, MD, PhD, Faculty of Medical Sciences, University of Kragujevac, S. Markovica 69, 34000 Kragujevac, Republic of Serbia, drmilena@yaho.com.

RESUMEN / SUMMARY: - Aim. To analyze the trends of pancreatic cancer mortality in Serbia. Methods. The study covered the population of Serbia in the period 1991 to 2010. Mortality trends were assessed by the joinpoint regression analysis by age and sex. Results. Age-standardized mortality rates ranged from 5.93 to 8.57 per 100 000 in men and from 3.51 to 5.79 per 100 000 in women. Pancreatic cancer mortality in all age groups was higher among men than among women. It was continuously increasing since 1991 by 1.6% (95% confidence interval [CI] 1.1 to 2.0) yearly in men and by 2.2% (95% CI 1.7 to 2.7) yearly in women. Changes in mortality were not significant in younger age groups for both sexes. In older men (≥ 55 years), mortality was increasing, although in age groups 70-74 and 80-84 the increase was not significant. In 65-69 years old men, the increase in mortality was significant only in the period 2004 to 2010. In ≥ 50 years old women, mortality significantly increased from 1991

onward. In 75-79 years old women, a non-significant decrease in the period 1991 to 2000 was followed by a significant increase from 2000 to 2010. Conclusion. Serbia is one of the countries with the highest pancreatic cancer mortality in the world, with increasing mortality trend in both sexes and in most age groups.

[280]

TÍTULO / TITLE: - Expression and clinical significance of complement C3, complement C4b1 and apolipoprotein E in pancreatic cancer.

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

REVISTA / JOURNAL: - Oncol Lett. 2013 Jul;6(1):43-48. Epub 2013 Apr 30.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1326](#)

AUTORES / AUTHORS: - Chen J; Wu W; Zhen C; Zhou H; Yang R; Chen L; Hu L

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Anhui Provincial Hospital Affiliated to Anhui Medical University, Hefei, Anhui 230001, P.R. China.

RESUMEN / SUMMARY: - Pancreatic cancer (PC) remains a devastating disease with a five-year survival rate of <5%. The difficulty in making an early diagnosis and the frequent occurrence of metastasis are important reasons for this poor prognosis. In China, the incidence of PC has been increasing steadily. Therefore, the present study aimed to identify effective markers in the early and advanced stages of PC. The expression levels of complement C3, complement C4b1 and apolipoprotein E (ApoE) in the various stages of PC were assessed by immunohistochemistry, RT-PCR and western blotting. Additionally, the statistical significance of the results was analyzed. The expression levels of complement C3, complement C4b1 and apoE were higher in PC compared with normal pancreatic tissues. No correlations were observed between complement C3 and tumor TNM staging or lymph node metastasis. However, complement C4b1 and apoE were markedly correlated with tumor TNM staging and lymph node metastasis. Complement C3 may be used as a marker for the diagnosis of early-stage PC, while complement C4b1 and apoE are closely correlated with tumor development, reflecting the biological behavior of PC, and thus may be used as diagnostic markers of advanced PC.

[281]

TÍTULO / TITLE: - Arsenic trioxide inhibits viability of pancreatic cancer stem cells in culture and in a xenograft model via binding to SHH-Gli.

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

REVISTA / JOURNAL: - Onco Targets Ther. 2013 Aug 19;6:1129-38. doi: 10.2147/OTT.S49148.

●● Enlace al texto completo (gratis o de pago) [2147/OTT.S49148](#)

AUTORES / AUTHORS: - Han JB; Sang F; Chang JJ; Hua YQ; Shi WD; Tang LH; Liu LM

INSTITUCIÓN / INSTITUTION: - Department of integrative Oncology, Fudan University Shanghai Cancer Center, Shanghai, People's Republic of China ; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, People's Republic of China.

RESUMEN / SUMMARY: - OBJECTIVE: Overexpression of the sonic hedgehog (SHH) signaling pathway is an essential characteristic of pancreatic cancer stem cells (PCSCs) and arsenic trioxide (ATO) is described as a SHH inhibitor. This study evaluates whether ATO has the potential to inhibit viability of PCSCs via binding to SHH-Gli proteins. METHODS: Cell counting kit-8 and flow cytometry were used for analyzing apoptosis in cells in vitro. The animal model was an athymic nude mouse model bearing subcutaneous xenografts of SW1990 pancreatic cancer cells. The terminal deoxynucleotidyl transferase dUTP nick end labeling assay and immunohistochemistry were used for tumor tissue analysis. The interaction between Gli1 and ATO was examined by a confocal system and an ultraviolet absorption spectrum assay. RESULTS: ATO induced apoptosis in pancreatic cancer cells, especially CD24(+)CD44(+) cells in vitro. Combination treatment of ATO and low dose gemcitabine inhibited tumor growth by 60.9% (P = 0.004), and decreased the expression of CD24, CD44, and aldehyde dehydrogenase 1 family, member A1 significantly in vivo. ATO changed the structure of the recombinant Gli1 zinc finger peptides in a cell-free condition and the binding action of ATO to recombinant Gli1 was observed in cultured pancreatic cancer cells. CONCLUSION: ATO may have the potential to inhibit viability of PCSCs via binding to SHH-Gli proteins in vitro and in vivo.

[282]

TÍTULO / TITLE: - Cucurmosin induces the apoptosis of human pancreatic cancer CFPAC-1 cells by inactivating the PDGFR-beta signalling pathway.

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

REVISTA / JOURNAL: - Pharmacol Rep. 2013;65(3):682-8.

AUTORES / AUTHORS: - Xie J; Wang C; Zhang B; Yang A; Yin Q; Huang H; Chen M

INSTITUCIÓN / INSTITUTION: - Department of Pharmacology, Fujian Medical University, Fuzhou 350004, Fujian, China. xiejm1@sina.com or hhuang2@aliyun.com.

RESUMEN / SUMMARY: - Background: Pancreatic cancer treatment is limited and effective drugs are needed. We investigated cucurmosin (CUS)-induced apoptosis in cystic fibrosis pancreatic adenocarcinoma cells (CFPAC-1) and a possible mechanism of action to evaluate the clinical application potential of this new Type I ribosome-inactivating protein. Methods: We analyzed the growth inhibition and apoptosis of CFPAC-1 cells via methylthiazol tetrazolium assay and fluorescence-activated cell sorting. Western blot was used to analyze the protein levels of caspase 3, bcl-2, caspase 9, platelet-derived growth factor receptor (PDGFR)-beta, PI3K, Akt, p-Akt, the mammalian target of rapamycin (mTOR), p-mTOR, P70S6K-alpha, p-P70S6K-alpha, 4E-BP1, p-4E-BP1 and p-Bad after CUS intervention. The mRNA expression of PDGFR-beta

was analyzed using reverse transcription polymerase chain reaction. Results: CUS inhibited the proliferation of pancreatic cancer cells. The induction of apoptosis depended on the CUS dose and incubation time. The drug inhibited all of the examined proteins in the PI3K/Akt/mTOR signalling pathway and induced the active fragments of caspase 3 and caspase 9. CUS downregulated PDGFR-beta expression but no significant change was observed at the mRNA level. Conclusion: CUS strongly inhibits the growth of CFPAC-1 by inducing cell apoptosis. CUS downregulated the expression of PDGFR-beta at the protein level and induced the apoptosis of CFPAC-1 through the PI3K/Akt/mTOR signalling pathway.

[283]

TÍTULO / TITLE: - Role of CXCL12/CXCR4 signaling axis in pancreatic cancer.

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

REVISTA / JOURNAL: - Chin Med J (Engl). 2013 Sep;126(17):3371-4.

AUTORES / AUTHORS: - Wu PF; Lu ZP; Cai BB; Tian L; Zou C; Jiang KR; Miao Y

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, First Affiliated Hospital with Nanjing Medical University, Nanjing, China.

RESUMEN / SUMMARY: - OBJECTIVE: This review focuses on the state-of-the-art of CXCL12/CXCR4 signaling axis in pancreatic cancer and its role in tumor progression. DATA SOURCES: Relevant articles published in English were identified by searching in Pubmed from 1997 to 2013, with keywords "CXCL12", "CXCR4" and "pancreatic cancer". Important references from selected articles were also retrieved. STUDY SELECTION: Articles about CXCL12/CXCR4 signaling axis in pancreatic cancer and relevant mechanisms were selected. RESULTS: Pancreatic cancer has been one of the most lethal human malignancies, with median survival less than one year and overall 5-year survival only 6%. Tumor cells from pancreatic cancer express high level of CXCR4. CXCL12, the ligand for CXCR4, is extensively secreted by neighboring stromal cells and other distant organs. CXCL12 primarily binds to CXCR4, induces intracellular signaling through several divergent pathways, which are involved in progression and metastasis of pancreatic cancer. CONCLUSIONS: CXCL12/CXCR4 signaling axis may play an important role in the communication between pancreatic cancer cells and their microenvironment, which may have effect on tumor proliferation, invasion, angiogenesis, metastasis and chemoresistance. CXCL12/CXCR4 signaling axis may serves as a novel therapeutic target for pancreatic cancer.

[284]

TÍTULO / TITLE: - Photothermal ablation of pancreatic cancer cells with hybrid iron-oxide core gold-shell nanoparticles.

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

REVISTA / JOURNAL: - Int J Nanomedicine. 2013;8:3437-46. doi: 10.2147/IJN.S47585.
Epub 2013 Sep 6.

●● Enlace al texto completo (gratis o de pago) [2147/IJN.S47585](https://doi.org/10.2147/IJN.S47585)

AUTORES / AUTHORS: - Guo Y; Zhang Z; Kim DH; Li W; Nicolai J; Procissi D; Huan Y; Han G; Omary RA; Larson AC

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Northwestern University, Chicago, IL, USA.

RESUMEN / SUMMARY: - **PURPOSE:** Photothermal ablation is a minimally invasive approach, which typically involves delivery of photothermal sensitizers to targeted tissues. The purpose of our study was to demonstrate that gold nanoparticles are phagocytosed by pancreatic cancer cells, thus permitting magnetic resonance imaging (MRI) of sensitizer delivery and photothermal ablation. **PATIENTS AND METHODS:** Iron-oxide core/gold-shell nanoparticles (GoldMag[®], 30 nm diameter; Xi'an GoldMag Biotechnology Co, Xi'an, People's Republic of China) were used. In a 96-well plate, 3 x 10⁴ PANC-1 (human pancreatic cancer cell line) cells were placed. GoldMag (0, 25, or 50 µg/mL) was added to each well and 24 hours allowed for cellular uptake. Samples were then divided into two groups: one treated with photothermal ablation (7.9 W/cm²) for 5 minutes, the other not treated. Photothermal ablation was performed using laser system (BWF5; B&W Tek, Inc, Newark, DE, USA). Intraprocedural temperature changes were measured using a fiber optic temperature probe (FTP-LN2; Photon Control Inc, Burnaby, BC, Canada). After 24 hours, the remaining number of viable cells was counted using trypan blue staining; cell proliferation percentage was calculated based on the total number of viable cells after treatment compared with control. MRI of GoldMag uptake was performed using a 7.0T ClinScan system (Bruker BioSpin, Ettlingen, Germany). **RESULTS:** Temperature curves demonstrated that with increased GoldMag uptake, laser irradiation produced higher temperature elevations in the corresponding samples; temperature elevations of 12.89 degrees C, 35.16 degrees C, and 79.51 degrees C were achieved for 0, 25, and 50 µg/mL GoldMag. Without photothermal ablation, the cell proliferation percentage changed from 100% to 71.3% and 47.0% for cells treated with 25 and 50 µg/mL GoldMag. Photothermal ablation of PANC-1 cells demonstrated an effective treatment response, specifically a reduction to only 61%, 21.9%, and 2.3% cell proliferation for cells treated with 0, 25, and 50 µg/mL GoldMag. MRI was able to visualize GoldMag uptake within PANC-1 cells. **CONCLUSION:** Our findings suggest that photothermal ablation may be effective in the treatment of pancreatic cancer. GoldMag nanoparticles could serve as photothermal sensitizers, and MRI is feasible to quantify delivery.

[285]

TÍTULO / TITLE: - Combination of siRNA-directed Kras oncogene silencing and arsenic-induced apoptosis using a nanomedicine strategy for the effective treatment of pancreatic cancer.

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

REVISTA / JOURNAL: - Nanomedicine. 2013 Sep 9. pii: S1549-9634(13)00469-3. doi: 10.1016/j.nano.2013.08.007.

●● Enlace al texto completo (gratis o de pago) [1016/j.nano.2013.08.007](#)

AUTORES / AUTHORS: - Zeng L; Li J; Wang Y; Qian C; Chen Y; Zhang Q; Wu W; Lin Z; Liang J; Shuai X; Huang K

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, The Second Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; Department of Oncology, The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, China.

RESUMEN / SUMMARY: - The synergetic inhibitory effects on human pancreatic cancer by nanoparticle-mediated siRNA and arsenic therapy were investigated both in vitro and in vivo. Poly(ethylene glycol)-block-poly(L-lysine) were prepared to form siRNA-complexed polyplex and poly(ethylene glycol)-block-poly(DL-lactide) were prepared to form arsenic-encapsulated vesicle, respectively. Down-regulation of the mutant Kras gene by siRNA caused defective abilities of proliferation, clonal formation, migration, and invasion of pancreatic cancer cells, as well as cell cycle arrest at the G0/G1 phase, which substantially enhanced the apoptosis-inducing effect of arsenic administration. Consequently, co-administration of the two nanomedicines encapsulating siRNA or arsenic showed ideal tumor growth inhibition both in vitro and in vivo as a result of synergistic effect of the siRNA-directed Kras oncogene silencing and arsenic-induced cell apoptosis. These results suggest that the combination of mutant Kras gene silencing and arsenic therapy using nanoparticle-mediated delivery strategy is promising for pancreatic cancer treatment.

[286]

TÍTULO / TITLE: - In vivo activity and pharmacokinetics of nemorosone on pancreatic cancer xenografts.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 5;8(9):e74555. doi: 10.1371/journal.pone.0074555.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0074555](#)

AUTORES / AUTHORS: - Wolf RJ; Hilger RA; Hoheisel JD; Werner J; Holtrup F

INSTITUCIÓN / INSTITUTION: - Division of Functional Genome Analysis, German Cancer Research Center (DKFZ), Heidelberg, Germany ; Department of General Surgery, University of Heidelberg, Heidelberg, Germany.

RESUMEN / SUMMARY: - Pancreatic cancer is one of the leading cancer-related causes of death in the western world with an urgent need for new treatment strategies. Recently, hyperforin and nemorosone have been described as promising anti-cancer lead compounds. While hyperforin has been thoroughly investigated in vitro and in vivo, in vivo data for nemorosone are still missing. Thus, we investigated the growth-inhibitory potential of nemorosone on pancreatic cancer xenografts in NMRI nu/nu

mice and determined basic pharmacokinetic parameters. Xenograft tumors were treated with nemorosone and gemcitabine, the current standard of care. Tumor sections were subjected to H&E as well as caspase 3 and Ki-67 staining. Nemorosone plasma kinetics were determined by HPLC and mass spectrometry. Induction of CYP3A4 and other metabolizing enzymes by nemorosone and hyperforin was tested on primary hepatocytes using qRT-PCR. At a dose of 50 mg/kg nemorosone per day, a significant growth-inhibitory effect was observed in pancreatic cancer xenografts. The compound was well tolerated and rapidly absorbed into the bloodstream with a half-life of approximately 30 min. Different metabolites were detected, possibly resembling CYP3A4-independent oxidation products. It is concluded that nemorosone is a potential anti-cancer lead compound with good bioavailability, little side-effects and promising growth-inhibitory effects, thus representing a valuable compound for a combination therapy approach.

[287]

TÍTULO / TITLE: - MicroRNA-221 Mediates the Effects of PDGF-BB on Migration, Proliferation, and the Epithelial-Mesenchymal Transition in Pancreatic Cancer Cells.

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

REVISTA / JOURNAL: - PLoS One. 2013;8(8):e71309. doi: 10.1371/journal.pone.0071309.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0071309](#)

AUTORES / AUTHORS: - Su A; He S; Tian B; Hu W; Zhang Z

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliopancreatic Surgery, West China Hospital, Sichuan University, Chengdu, P. R. China.

RESUMEN / SUMMARY: - The platelet-derived growth factor (PDGF) signaling pathway has been found to play important roles in the development and progression of human cancers by regulating the processes of cell proliferation, apoptosis, migration, invasion, metastasis, and the acquisition of the epithelial-mesenchymal transition (EMT) phenotype. Moreover, PDGF signaling has also been found to alter the expression profile of miRNAs, leading to the reversal of EMT phenotype. Although the role of miRNAs in cancer has been documented, there are very few studies documenting the cellular consequences of targeted re-expression of specific miRNAs. Therefore, we investigated whether the treatment of human pancreatic cancer cells with PDGF could alter the expression profile of miRNAs, and we also assessed the cellular consequences. Our study demonstrates that miR-221 is essential for the PDGF-mediated EMT phenotype, migration, and growth of pancreatic cancer cells. Down-regulation of TRPS1 by miR-221 is critical for PDGF-mediated acquisition of the EMT phenotype. Additionally, the PDGF-dependent increase in cell proliferation appears to be mediated by inhibition of a specific target of miR-221 and down-regulation of p27Kip1.

[288]

TÍTULO / TITLE: - Application of biochemical markers CA 19-9, CEA and C-reactive protein in diagnosis of malicious and benign pancreatic tumors.

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

REVISTA / JOURNAL: - Arch Med Sci. 2013 Aug 30;9(4):677-83. doi: 10.5114/aoms.2013.36899. Epub 2013 Aug 8.

●● Enlace al texto completo (gratis o de pago) [5114/aoms.2013.36899](#)

AUTORES / AUTHORS: - Smigielski JA; Piskorz L; Wawrzycki M; Dobielski P; Pikala M; Jablonski S; Brocki M

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, General Surgery and Oncology, Medical University of Lodz, Poland.

RESUMEN / SUMMARY: - INTRODUCTION: We would save many lives and spare a lot of suffering if we could only detect and accurately determine the character and TMN staging of pancreatic tumors (PTs). With improved diagnosis, we could offer specific treatment that would result in better treatment outcome. The aim of study was to determine the significance of neoplastic markers CA 19-9 and CEA for prognosis in inflammatory and carcinomatous PTs. MATERIAL AND METHODS: We based our research upon a group of 170 patients. The patients were treated in our Oncologic Surgery Department from January 2007 to December 2010 for PTs. The patients were divided into four groups depending on the character of the tumor and underwent the following treatments: group 1 - 34 patients with carcinoma of the ampulla of Vater, group 2 - 64 patients with PTs at different stages (1, 2, 3) according to TMN classification, group 3 - 62 patients with PTs at stage 4 on the TMN scale (unresectable tumors), group 4 - 28 patients with inflammatory PTs. RESULTS: The results of Ca 19-9 in group 2 were 736.00 (25-75% 220.40-4285.00) ng/ml before surgery, 53.00 (25-75% 12.60-84.00) ng/ml in the 7 days after surgery, 29.4 (25-75% 7.90-113.00) ng/ml at day 30, and 119.00 (25-75% 96.30-621.00) ng/ml 3 months after the operation. These results were significantly higher than the control group but were significantly lower than the results for group 3 (unresectable tumors). The highest average concentration and median for CA 19-9 and CEA were noted in patients with unresectable PTs (the 3rd group). The average concentration for CEA was lowest in group 4, but much higher than the lab limits. CONCLUSIONS: The sensitivity of the CA 19-9 marker may be as high as 88%. Values of CA 19-9 above 852 U/ml may indicate TNM stage 4, consistent with an unresectable PT. In the cases where CA 19-9 is within normal limits but C-reactive protein is above normal limits (often thirty times the upper limit), in comparison to the control group and to patients with pancreatic neoplasms, strong consideration should be given towards the inflammatory characteristics of the pancreatic changes and conservative treatment should be applied.

[289]

TÍTULO / TITLE: - The marine natural product manzamine targets vacuolar ATPases and inhibits autophagy in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Mar Drugs. 2013 Sep 17;11(9):3500-16. doi: 10.3390/md11093500.

●● Enlace al texto completo (gratis o de pago) [3390/md11093500](#)

AUTORES / AUTHORS: - Kallifatidis G; Hoepfner D; Jaeg T; Guzman EA; Wright AE

INSTITUCIÓN / INSTITUTION: - Marine Biomedical and Biotechnology Research Program, Harbor Branch Oceanographic Institute, Florida Atlantic University, 5600 US 1 North, Fort Pierce, FL 34946, USA. eguzman9@hboi.fau.edu.

RESUMEN / SUMMARY: - Manzamine A, a member of the manzamine alkaloids, was originally isolated from marine sponges of the genus Haliclona. It was recently shown to have activity against pancreatic cancer cells, but the precise mechanism of action remained unclear. To further our understanding of the mechanism of action of manzamine A, chemogenomic profiling in the yeast *S. cerevisiae* was performed, suggesting that manzamine A is an uncoupler of vacuolar ATPases. Fluorescence microscopy confirmed this effect on yeast vacuoles, where manzamine A produced a phenotype very similar to that of the established v-ATPase inhibitor bafilomycin A1. In pancreatic cancer cells, 10 µM manzamine A affected vacuolar ATPase activity and significantly increased the level of autophagosome marker LC3-II and p62/SQSTM1 as observed by western blot analysis. Treatment with manzamine A in combination with bafilomycin A1 (inhibitor of autophagosome-lysosome fusion) did not change the levels of LC3-II when compared to cells treated with bafilomycin A1 alone, suggesting that manzamine A is a potential inhibitor of autophagy by preventing autophagosome turnover. As autophagy is essential for pancreatic tumor growth, blocking this pathway with manzamine A suggests a promising strategy for the treatment of pancreatic cancer.

[290]

TÍTULO / TITLE: - Collagen XV Inhibits Epithelial to Mesenchymal Transition in Pancreatic Adenocarcinoma Cells.

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

REVISTA / JOURNAL: - PLoS One. 2013 Aug 22;8(8):e72250. doi: 10.1371/journal.pone.0072250.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0072250](#)

AUTORES / AUTHORS: - Clementz AG; Mutolo MJ; Leir SH; Morris KJ; Kucybala K; Harris H; Harris A

INSTITUCIÓN / INSTITUTION: - Human Molecular Genetics Program, Lurie Children's Research Center, Chicago, Illinois, United States of America ; Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, Illinois, United States of America.

RESUMEN / SUMMARY: - Collagen XV (COLXV) is a secreted non-fibrillar collagen found within basement membrane (BM) zones of the extracellular matrix (ECM). Its ability to alter cellular growth in vitro and to reduce tumor burden and increase survival in vivo

support a role as a tumor suppressor. Loss of COLXV during the progression of several aggressive cancers precedes basement membrane invasion and metastasis. The resultant lack of COLXV subjacent to the basement membrane and subsequent loss of its interactions with other proteins in this zone may directly impact tumor progression. Here we show that COLXV significantly reduces invasion of pancreatic adenocarcinoma cells through a collagen I (COLI) matrix. Moreover, we demonstrate that epithelial to mesenchymal transition (EMT) in these cells, which is recapitulated in vitro by cell scattering on a COLI substrate, is inhibited by over-expression of COLXV. We identify critical collagen-binding surface receptors on the tumor cells, including the discoidin domain receptor 1 (DDR1) and E-Cadherin (E-Cad), which interact with COLXV and appear to mediate its function. In the presence of COLXV, the intracellular redistribution of E-Cad from the cell periphery, which is associated with COLI-activated EMT, is inhibited and concurrently, DDR1 signaling is suppressed. Furthermore, continuous exposure of the pancreatic adenocarcinoma cells to high levels of COLXV suppresses endogenous levels of N-Cadherin (N-Cad). These data reveal a novel mechanism whereby COLXV can function as a tumor suppressor in the basement membrane zone.

[291]

TÍTULO / TITLE: - Pancreatic cancer-associated stellate cells: A viable target for reducing immunosuppression in the tumor microenvironment.

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

REVISTA / JOURNAL: - Oncoimmunology. 2013 Jul 1;2(7):e24891. Epub 2013 May 7.

●● Enlace al texto completo (gratis o de pago) [4161/onci.24891](#)

AUTORES / AUTHORS: - Mace TA; Bloomston M; Lesinski GB

INSTITUCIÓN / INSTITUTION: - Division of Medical Oncology; Department of Internal Medicine; The Ohio State University; Columbus, OH USA.

RESUMEN / SUMMARY: - Pancreatic cancer-associated stellate cells secrete soluble factors, such as interleukin-6 (IL-6), that promote the accumulation of myeloid-derived suppressor cells via a signal transducer and activator of transcription 3 (STAT3)-dependent mechanism. Targeting components of the IL-6/JAK/STAT3 signaling axis within the tumor stroma could therefore inhibit local immunosuppression and improve the efficacy of immunotherapeutic regimens against pancreatic cancer.

[292]

TÍTULO / TITLE: - Effect of Photofrin-mediated photocytotoxicity on a panel of human pancreatic cancer cells.

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

REVISTA / JOURNAL: - Photodiagnosis Photodyn Ther. 2013 Sep;10(3):244-51. doi: 10.1016/j.pdpdt.2012.11.001. Epub 2013 Jan 30.

●● Enlace al texto completo (gratis o de pago) [1016/j.pdpdt.2012.11.001](#)

AUTORES / AUTHORS: - Wang LW; Huang Z; Lin H; Li ZS; Hetzel F; Liu B

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Changhai Hospital, The Second Military Medical University, Shanghai, China; Division of Gastroenterology & Hepatology, University of Colorado Denver, Aurora, CO, USA; Department of Pathology, University of Colorado Denver, Aurora, CO, USA.

RESUMEN / SUMMARY: - BACKGROUND AND OBJECTIVE: Pancreatic cancer is a leading cause of cancer-related deaths in men and women. Early clinical studies suggest that photodynamic therapy (PDT) might be a useful modality in the management of this deadly disease. In this study, the photocytotoxicity of Photofrin-mediated PDT on different human pancreatic cancer cells (BxPc-3, HPAF-II, Mia PaCa-2, MPanc-96, PANC-1 and PL-45) was examined. MATERIALS AND METHODS: After co-incubating cancer cells with Photofrin (0-10µg/ml) for 4h, the cells were irradiated with 0-6J/cm² of 630nm light. The effect of Photofrin PDT on the survival of cells were examined using tetrazolium-based colorimetric assay and clonogenic assay. PDT-induced apoptosis was analyzed by flow cytometry. Expressions of apoptosis-related proteins were determined by western blot analysis. RESULTS: Photofrin PDT strongly inhibited the survival of pancreatic cancer cells. A small portion of cells (<15%) underwent apoptosis 24h after PDT at LD50. Cleavage of caspase-3, caspase-8, caspase-9 and PARP after PDT were also confirmed. BxPc-3, Mia PaCa-2, MPanc-96, and PANC-1 cells were more sensitive and HPAF-II and PL-45 cells less sensitive. CONCLUSION: Photofrin PDT can induce apoptosis and inhibit survival of human pancreatic cancer cells.

[293]

TÍTULO / TITLE: - SOX2 promotes dedifferentiation and imparts stem cell-like features to pancreatic cancer cells.

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

REVISTA / JOURNAL: - Oncogenesis. 2013 Aug 5;2:e61. doi: 10.1038/oncsis.2013.23.

●● Enlace al texto completo (gratis o de pago) [1038/oncsis.2013.23](#)

AUTORES / AUTHORS: - Herreros-Villanueva M; Zhang JS; Koenig A; Abel EV; Smyrk TC; Bamlet WR; de Narvajas AA; Gomez TS; Simeone DM; Bujanda L; Billadeau DD

INSTITUCIÓN / INSTITUTION: - 1] Division of Oncology Research, Schulze Center for Novel Therapeutics, College of Medicine, Mayo Clinic, Rochester, MN, USA [2] Department of Gastroenterology, Centro de Investigacion Biomedica en Red de Enfermedades Hepaticas y Digestivas (CIBERehd), Hospital Donostia/Instituto Biodonostia, Universidad del Pais Vasco UPV/EHU, San Sebastian, España.

RESUMEN / SUMMARY: - SOX2 (Sex-determining region Y (SRY)-Box2) has important functions during embryonic development and is involved in cancer stem cell (CSC) maintenance, in which it impairs cell growth and tumorigenicity. However, the function of SOX2 in pancreatic cancer cells is unclear. The objective of this study was to analyze SOX2 expression in human pancreatic tumors and determine the role of SOX2

in pancreatic cancer cells regulating CSC properties. In this report, we show that SOX2 is not expressed in normal pancreatic acinar or ductal cells. However, ectopic expression of SOX2 is observed in 19.3% of human pancreatic tumors. SOX2 knockdown in pancreatic cancer cells results in cell growth inhibition via cell cycle arrest associated with p21(Cip1) and p27(Kip1) induction, whereas SOX2 overexpression promotes S-phase entry and cell proliferation associated with cyclin D3 induction. SOX2 expression is associated with increased levels of the pancreatic CSC markers ALDH1, ESA and CD44. Importantly, we show that SOX2 is enriched in the ESA(+)/CD44(+) CSC population from two different patient samples. Moreover, we show that SOX2 directly binds to the Snail, Slug and Twist promoters, leading to a loss of E-Cadherin and ZO-1 expression. Taken together, our findings show that SOX2 is aberrantly expressed in pancreatic cancer and contributes to cell proliferation and stemness/dedifferentiation through the regulation of a set of genes controlling G1/S transition and epithelial-to-mesenchymal transition (EMT) phenotype, suggesting that targeting SOX2-positive cancer cells could be a promising therapeutic strategy.

[294]

TÍTULO / TITLE: - Protein Kinase C Zeta Regulates Human Pancreatic Cancer Cell Transformed Growth and Invasion through a STAT3-Dependent Mechanism.

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

REVISTA / JOURNAL: - PLoS One. 2013 Aug 28;8(8):e72061. doi: 10.1371/journal.pone.0072061.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0072061](#)

AUTORES / AUTHORS: - Butler AM; Scotti Buzhardt ML; Li S; Smith KE; Fields AP; Murray NR

INSTITUCIÓN / INSTITUTION: - Department of Cancer Biology, Mayo Clinic, Jacksonville, Florida, United States of America.

RESUMEN / SUMMARY: - Pancreatic cancer is a very aggressive disease with few therapeutic options. In this study, we investigate the role of protein kinase C zeta (PKCzeta) in pancreatic cancer cells. PKCzeta has been shown to act as either a tumor suppressor or tumor promoter depending upon the cellular context. We find that PKCzeta expression is either maintained or elevated in primary human pancreatic tumors, but is never lost, consistent with PKCzeta playing a promotive role in the pancreatic cancer phenotype. Genetic inhibition of PKCzeta reduced adherent growth, cell survival and anchorage-independent growth of human pancreatic cancer cells in vitro. Furthermore, PKCzeta inhibition reduced orthotopic tumor size in vivo by inhibiting tumor cell proliferation and increasing tumor necrosis. In addition, PKCzeta inhibition reduced tumor metastases in vivo, and caused a corresponding reduction in pancreatic cancer cell invasion in vitro. Signal transducer and activator of transcription 3 (STAT3) is often constitutively active in pancreatic cancer, and plays an important role in pancreatic cancer cell survival and metastasis. Interestingly, inhibition of

PKCzeta significantly reduced constitutive STAT3 activation in pancreatic cancer cells in vitro and in vivo. Pharmacologic inhibition of STAT3 mimicked the phenotype of PKCzeta inhibition, and expression of a constitutively active STAT3 construct rescued the transformed phenotype in PKCzeta-deficient cells. We conclude that PKCzeta is required for pancreatic cancer cell transformed growth and invasion in vitro and tumorigenesis in vivo, and that STAT3 is an important downstream mediator of the pro-carcinogenic effects of PKCzeta in pancreatic cancer cells.

[295]

TÍTULO / TITLE: - Pancreaticoduodenectomy versus local resection in the treatment of gastrointestinal stromal tumors of the duodenum.

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

REVISTA / JOURNAL: - World J Surg Oncol. 2013 Aug 14;11(1):196.

●● Enlace al texto completo (gratis o de pago) [1186/1477-7819-11-196](#)

AUTORES / AUTHORS: - Zhou B; Zhang M; Wu J; Yan S; Zhou J; Zheng S

RESUMEN / SUMMARY: - BACKGROUND: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms. However, duodenal GISTs comprise a small and rare subset and few studies have focused on them. We evaluated the surgical management of patients with duodenal GISTs treated by pancreaticoduodenectomy (PD) versus local resection (LR) in our institution and analyzed the postoperative outcomes. METHODS: This was a retrospective review of patients with duodenal GISTs managed in our institution from January 2006 to January 2012. Clinicopathologic findings and disease-free survival (DFS) of duodenal GIST patients were analyzed. RESULTS: A total of 48 patients were selected. The most common presentation was bleeding (60.4%), and the second portion of the duodenum (35.4%) was the most common dominant site. Of the patients, 34 (70.8%) underwent LR while 14 (29.2%) underwent PD. The surgical margins for all studied patients were free. Patients who ultimately underwent PD were more likely to present with a larger tumor (median size: PD, 6.3 cm vs LR, 4.0 cm; $P = 0.02$) and more commonly presented with a tumor in the second portion of the duodenum (second portion: PD, 64.3% vs LR, 23.5%; $P = 0.007$). The tumors treated by PD had a higher grade of risk compared with LR as defined by National Institutes of Health (NIH) criteria ($P = 0.019$). PD was significantly associated with a longer operation time and a longer hospital stay compared to LR ($P < 0.001$ and $P = 0.001$, respectively). In our study, the median follow-up period was 36 months (range: 0 to 81 months). The 1- and 3-year DFS was 100% and 88%, respectively. From multivariable analysis, the only significant factor associated with a worse DFS was an NIH high risk classification (hazard ratio = 4.24). CONCLUSIONS: The recurrence of duodenal GIST was correlated to tumor biology rather than type of operation. PD was associated with a longer hospital stay and longer operation time. Therefore, LR with clear surgical margins should be considered a

reliable and curative option for duodenal GIST and PD should be reserved for lesions not amenable to LR.

[296]

TÍTULO / TITLE: - Clinical and molecular characterization of HER2 amplified-pancreatic cancer.

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

REVISTA / JOURNAL: - Genome Med. 2013 Aug 31;5(8):78.

●● Enlace al texto completo (gratis o de pago) [1186/gm482](#)

AUTORES / AUTHORS: - Chou A; Waddell N; Cowley MJ; Gill AJ; Chang DK; Patch AM; Nones K; Wu J; Pinese M; Johns AL; Miller DK; Kassahn KS; Nagrial AM; Wasan H; Goldstein D; Toon CW; Chin V; Chantrill L; Humphris J; Mead RS; Rooman I; Samra JS; Pajic M; Musgrove EA; Pearson JV; Morey AL; Grimmond SM; Biankin AV

INSTITUCIÓN / INSTITUTION: - Kinghorn Cancer Centre and Garvan Institute of Medical Research, Darlinghurst, Sydney, Australia. amorey@stvincents.com.au.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is one of the most lethal and molecularly diverse malignancies. Repurposing of therapeutics that target specific molecular mechanisms in different disease types offers potential for rapid improvements in outcome. Although HER2 amplification occurs in pancreatic cancer, it is inadequately characterized to exploit the potential of anti-HER2 therapies. METHODS: HER2 amplification was detected and further analyzed using multiple genomic sequencing approaches. Standardized reference laboratory assays defined HER2 amplification in a large cohort of patients (n = 469) with pancreatic ductal adenocarcinoma (PDAC). RESULTS: An amplified inversion event (1 MB) was identified at the HER2 locus in a patient with PDAC. Using standardized laboratory assays, we established diagnostic criteria for HER2 amplification in PDAC, and observed a prevalence of 2%. Clinically, HER2- amplified PDAC was characterized by a lack of liver metastases, and a preponderance of lung and brain metastases. Excluding breast and gastric cancer, the incidence of HER2-amplified cancers in the USA is >22,000 per annum. CONCLUSIONS: HER2 amplification occurs in 2% of PDAC, and has distinct features with implications for clinical practice. The molecular heterogeneity of PDAC implies that even an incidence of 2% represents an attractive target for anti-HER2 therapies, as options for PDAC are limited. Recruiting patients based on HER2 amplification, rather than organ of origin, could make trials of anti-HER2 therapies feasible in less common cancer types.

[297]

TÍTULO / TITLE: - Analysis of PALB2 gene in BRCA1/BRCA2 negative Spanish hereditary breast/ovarian cancer families with pancreatic cancer cases.

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

REVISTA / JOURNAL: - PLoS One. 2013 Jul 23;8(7):e67538. doi: 10.1371/journal.pone.0067538. Print 2013.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0067538](https://doi.org/10.1371/journal.pone.0067538)

AUTORES / AUTHORS: - Blanco A; de la Hoya M; Osorio A; Diez O; Miramar MD; Infante M; Martinez-Bouzas C; Torres A; Lasa A; Llorca G; Brunet J; Grana B; Perez Segura P; Garcia MJ; Gutierrez-Enriquez S; Carracedo A; Tejada MI; Velasco EA; Calvo MT; Balmana J; Benitez J; Caldes T; Vega A

INSTITUCIÓN / INSTITUTION: - Fundacion Publica Galega de Medicina Xenomica-Servicio Galego de Saude, Grupo de Medicina Xenomica-Universidade de Santiago de Compostela, Spanish Network on Rare Diseases (CIBERER), Instituto de Investigaciones Sanitarias de Santiago, Santiago de Compostela, A Coruna, España.

RESUMEN / SUMMARY: - **BACKGROUND:** The PALB2 gene, also known as FANCD1, forms a bond and co-localizes with BRCA2 in DNA repair. Germline mutations in PALB2 have been identified in approximately 1% of familial breast cancer and 3-4% of familial pancreatic cancer. The goal of this study was to determine the prevalence of PALB2 mutations in a population of BRCA1/BRCA2 negative breast cancer patients selected from either a personal or family history of pancreatic cancer. **METHODS:** 132 non-BRCA1/BRCA2 breast/ovarian cancer families with at least one pancreatic cancer case were included in the study. PALB2 mutational analysis was performed by direct sequencing of all coding exons and intron/exon boundaries, as well as multiplex ligation-dependent probe amplification. **RESULTS:** Two PALB2 truncating mutations, the c.1653T>A (p.Tyr551Stop) previously reported, and c.3362del (p.Gly1121ValfsX3) which is a novel frameshift mutation, were identified. Moreover, several PALB2 variants were detected; some of them were predicted as pathological by bioinformatic analysis. Considering truncating mutations, the prevalence rate of our population of BRCA1/2-negative breast cancer patients with pancreatic cancer is 1.5%. **CONCLUSIONS:** The prevalence rate of PALB2 mutations in non-BRCA1/BRCA2 breast/ovarian cancer families, selected from either a personal or family pancreatic cancer history, is similar to that previously described for unselected breast/ovarian cancer families. Future research directed towards identifying other gene(s) involved in the development of breast/pancreatic cancer families is required.

[298]

TÍTULO / TITLE: - Pancreatic neuroendocrine tumors: approach to treatment with focus on sunitinib.

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

REVISTA / JOURNAL: - Therap Adv Gastroenterol. 2013 Sep;6(5):396-411. doi: 10.1177/1756283X13493878.

●● Enlace al texto completo (gratis o de pago) [1177_1756283X13493878](https://doi.org/10.1177/1756283X13493878) [pii]

●● Enlace al texto completo (gratis o de pago) [1177/1756283X13493878](https://doi.org/10.1177/1756283X13493878)

AUTORES / AUTHORS: - Vinik AI; Raymond E

INSTITUCIÓN / INSTITUTION: - Director of Research and Neuroendocrine Unit, EVMS Strelitz Diabetes Research Center, Eastern Virginia Medical School, 855 West Brambleton Avenue, Norfolk, VA 23510-1001, USA.

RESUMEN / SUMMARY: - Pancreatic neuroendocrine tumors (pNETs) are relatively rare malignancies. With secretory tumors such as insulinomas, vasoactive intestinal peptideomas, and gastrinomas, the hormone produced causes the symptom complex (e.g. hypoglycemia, peptic ulcer disease). With nonsecretory NETs, the clinical condition is determined by tumoral growth and metastasis. The course of metastatic pNETs may be indolent for several years but progression is often more rapid at later stages, leading to significant disability and a markedly negative impact on quality of life. Until recently, there were few effective systemic treatments for pNETs. Standard chemotherapy produces limited responses and has considerable toxicity. Somatostatin analogues control symptoms in some types of pNETs, but have not yet demonstrated antitumor activity. The recent introduction of targeted therapies, including the tyrosine kinase inhibitor sunitinib and the mammalian target of rapamycin inhibitor everolimus, yielded new opportunities for patients with advanced/metastatic pNETs. These drugs, which target key pathways in tumor proliferation and angiogenesis, provided clear clinical benefits in phase III clinical trials, including delayed tumor progression. The pivotal sunitinib phase III trial was discontinued prematurely due to higher rates of death and serious adverse events with placebo and greater progression-free survival (PFS) with sunitinib. In this trial, sunitinib demonstrated encouraging long-term responses as well as PFS and overall survival benefits, and an acceptable safety profile that allowed patients to preserve their quality of life. In every patient subgroup, including secretory and nonsecretory tumors, the hazard ratio for progression or death favored sunitinib. Circulating biomarkers are being investigated for the prediction and monitoring of responses to sunitinib. Although not fully evaluated in pNETs, biomarkers associated with response to sunitinib in several tumor types include soluble vascular endothelial growth factor receptor 2 and 3, interleukin 8, and stromal cell-derived factor 1alpha. Based on recent data, treatment algorithms have been updated for advanced and metastatic pNETs.

[299]

TÍTULO / TITLE: - TLR7 inhibition: A novel strategy for pancreatic cancer treatment?

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

REVISTA / JOURNAL: - JAKSTAT. 2013 Jan 1;2(1):e23011. doi: 10.4161/jkst.23011.

●● [Enlace al texto completo \(gratis o de pago\) 4161/jkst.23011](#)

AUTORES / AUTHORS: - Eigenbrod T; Dalpke AH

INSTITUCIÓN / INSTITUTION: - Department of Infectious Diseases; Medical Microbiology and Hygiene; University Heidelberg; Heidelberg, Germany.

RESUMEN / SUMMARY: - PANCREATIC DUCTAL ADENOCARCINOMA IS ASSOCIATED WITH A POOR PROGNOSIS: For local disease, the 5-y survival rate is approximately 20% and

median survival in locally advanced disease is only about 10 mo. Carcinogenesis is associated with chronic inflammation showing that innate immunity can be a double-edged sword. Here, we discuss recent findings of Ochi et al. in The Journal of Clinical Investigation who described a novel role for TLR7 in the development and progression of pancreatic cancer through interference with cell cycle regulation and by activation of multiple cell signaling pathways. Of note, inhibition of TLR7 signaling in a mouse p48Cre;Kras(G12D) pancreatic cancer model protected against tumor progression thus paving the road for TLR-blocking strategies to combat tumors.

[300]

TÍTULO / TITLE: - Predictive modeling of in vivo response to gemcitabine in pancreatic cancer.

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

REVISTA / JOURNAL: - PLoS Comput Biol. 2013 Sep;9(9):e1003231. doi: 10.1371/journal.pcbi.1003231. Epub 2013 Sep 19.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pcbi.1003231](#)

AUTORES / AUTHORS: - Lee JJ; Huang J; England CG; McNally LR; Frieboes HB

INSTITUCIÓN / INSTITUTION: - School of Medicine, University of Louisville, Louisville, Kentucky, United States of America.

RESUMEN / SUMMARY: - A clear contradiction exists between cytotoxic in-vitro studies demonstrating effectiveness of Gemcitabine to curtail pancreatic cancer and in-vivo studies failing to show Gemcitabine as an effective treatment. The outcome of chemotherapy in metastatic stages, where surgery is no longer viable, shows a 5-year survival <5%. It is apparent that in-vitro experiments, no matter how well designed, may fail to adequately represent the complex in-vivo microenvironmental and phenotypic characteristics of the cancer, including cell proliferation and apoptosis. We evaluate in-vitro cytotoxic data as an indicator of in-vivo treatment success using a mathematical model of tumor growth based on a dimensionless formulation describing tumor biology. Inputs to the model are obtained under optimal drug exposure conditions in-vitro. The model incorporates heterogeneous cell proliferation and death caused by spatial diffusion gradients of oxygen/nutrients due to inefficient vascularization and abundant stroma, and thus is able to simulate the effect of the microenvironment as a barrier to effective nutrient and drug delivery. Analysis of the mathematical model indicates the pancreatic tumors to be mostly resistant to Gemcitabine treatment in-vivo. The model results are confirmed with experiments in live mice, which indicate uninhibited tumor proliferation and metastasis with Gemcitabine treatment. By extracting mathematical model parameter values for proliferation and death from monolayer in-vitro cytotoxicity experiments with pancreatic cancer cells, and simulating the effects of spatial diffusion, we use the model to predict the drug response in-vivo, beyond what would have been expected from sole consideration of the cancer intrinsic resistance. We conclude that this

integrated experimental/computational approach may enhance understanding of pancreatic cancer behavior and its response to various chemotherapies, and, further, that such an approach could predict resistance based on pharmacokinetic measurements with the goal to maximize effective treatment strategies.

[301]

TÍTULO / TITLE: - The role of Mediterranean diet on the risk of pancreatic cancer.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Sep 3;109(5):1360-6. doi: 10.1038/bjc.2013.345. Epub 2013 Aug 8.

●● Enlace al texto completo (gratis o de pago) [1038/bjc.2013.345](#)

AUTORES / AUTHORS: - Bosetti C; Turati F; Pont AD; Ferraroni M; Polesel J; Negri E; Serraino D; Talamini R; Vecchia CL; Zeegers MP

INSTITUCIÓN / INSTITUTION: - Department of Epidemiology, IRCCS-Istituto di Ricerche Farmacologiche 'Mario Negri', Milan, Italy.

RESUMEN / SUMMARY: - Background:The Mediterranean diet has been shown to have a beneficial role on various neoplasms, but data are scanty on pancreatic cancer.Methods:We analysed data from two case-control studies conducted in Italy between 1983 and 2008, including 362 and 326 pancreatic cancer cases and 1552 and 652 hospital-controls, respectively. A Mediterranean Diet Score (MDS) summarising major characteristics of the Mediterranean diet was used in the two studies separately and overall. Two further scores of adherence to the Mediterranean diet were applied in the second study only, the Mediterranean Dietary Pattern Adherence Index (MDP) and the Mediterranean Adequacy Index (MAI).Results:Odds ratios (ORs) for increasing levels of the scores (i.e., increasing adherence) were estimated using multiple logistic regression models. Odds ratio for a MDS score ≥ 6 compared with < 3 was 0.57 (95% confidence interval (CI) 0.34-0.95) in the first study, 0.51 (95% CI 0.29-0.92) in the second study, and 0.48 (95% CI 0.35-0.67) overall. A trend of decreasing risk was observed also for the MDP and MAI the ORs for the highest vs the lowest quintile being 0.44 (95% CI 0.27-0.73) for MDP and 0.68 (95% CI 0.42-1.11) for the MAI. The results were consistent across strata of age, sex, education, body mass index, alcohol drinking, tobacco smoking, and diabetes.Conclusion:Our study provides evidence that a priori-defined scores measuring adherence to the Mediterranean diet are favourably associated with pancreatic cancer risk.

[302]

TÍTULO / TITLE: - Application of concave microwells to pancreatic tumor spheroids enabling anticancer drug evaluation in a clinically relevant drug resistance model.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 10;8(9):e73345. doi: 10.1371/journal.pone.0073345.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0073345](https://doi.org/10.1371/journal.pone.0073345)

AUTORES / AUTHORS: - Yeon SE; No da Y; Lee SH; Nam SW; Oh IH; Lee J; Kuh HJ

INSTITUCIÓN / INSTITUTION: - Lab of Onco-Pharmacology and Experimental Therapeutics, Department of Biomedical Sciences, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea.

RESUMEN / SUMMARY: - Intrinsic drug resistance of pancreatic ductal adenocarcinoma (PDAC) warrants studies using models that are more clinically relevant for identifying novel resistance mechanisms as well as for drug development. Tumor spheroids (TS) mimic in vivo tumor conditions associated with multicellular resistance and represent a promising model for efficient drug screening, however, pancreatic cancer cells often fail to form spheroids using conventional methods such as liquid overlay. This study describes the induction of TS of human pancreatic cancer cells (Panc-1, Aspc-1, Capan-2) in concave polydimethylsiloxane (PDMS) microwell plates and evaluation of their usefulness as an anticancer efficacy test model. All three cell lines showed TS formation with varying degree of necrosis inside TS. Among these, Panc-1 spheroid with spherical morphology, a rather rough surface, and unique adhesion structures were successfully produced with no notable necrosis in concave microwell plates. Panc-1 TS contained growth factors or enzymes such as TGF-beta1, CTGF, and MT1-MMP, and extracellular matrix proteins such as collagen type I, fibronectin, and laminin. Panc-1 cells grown as TS showed changes in stem cell populations and in expression levels of miRNAs that may play roles in chemoresistance. Visualization of drug penetration and detection of viability indicators, such as Ki-67 and MitoSOX, were optimized for TS for quantitative analysis. Water-soluble tetrazolium (MTS) and acid phosphatase (APH) assays were also successfully optimized. Overall, we demonstrated that concave PDMS microwell plates are a novel platform for preparation of TS of weakly aggregating cells and that Panc-1 spheroids may represent a novel three-dimensional model for anti-pancreatic cancer drug screening.

[303]

TÍTULO / TITLE: - Do hENT1 and RRM1 predict the clinical benefit of gemcitabine in pancreatic cancer?

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

REVISTA / JOURNAL: - Biomark Med. 2013 Aug;7(4):663-71. doi: 10.2217/bmm.13.48.

●● Enlace al texto completo (gratis o de pago) [2217/bmm.13.48](https://doi.org/10.2217/bmm.13.48)

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INSTITUCIÓN / INSTITUTION: - University of Lyon, F-69000 Lyon, France. lars-petter.jordheim@univ-lyon1.fr

RESUMEN / SUMMARY: - Gemcitabine is a nucleoside analog that is indicated in the treatment of pancreatic cancer. In order to provide a better use of this drug, the search for immunohistological markers is a hot topic in the field of pancreatic cancer. In particular, the use of nucleoside transporter hENT1 and the intracellular target of

gemcitabine RRM1 are current subjects for discussion. We have analyzed the majority of studies of hENT1 and RRM1 on pancreatic cancer, and will discuss the further directions that might be followed in order to integrate these proteins in routine clinical practice. The data that is currently available would benefit from the completion of well-designed randomized trials in order to confirm the clinical value of hENT1 and RRM1 as biomarkers in pancreatic cancer patients.

[304]

TÍTULO / TITLE: - Pattern and Clinical Predictors of Lymph Node Involvement in Nonfunctioning Pancreatic Neuroendocrine Tumors (NF-PanNETs).

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

REVISTA / JOURNAL: - JAMA. %8?(3k+]3s <http://jama.ama-assn.org/search.dtl> ●●
JAMA: <> Surg. 2013 Aug 28. doi: 10.1001/jamasurg.2013.3376.

●● Enlace al texto completo (gratis o de pago) 1001/jamasurg.2013.3376

AUTORES / AUTHORS: - Partelli S; Gaujoux S; Boninsegna L; Cherif R; Crippa S; Couvelard A; Scarpa A; Ruzsniwski P; Sauvanet A; Falconi M

INSTITUCIÓN / INSTITUTION: - Departments of Surgery and Pathology, University of Verona, Verona, Italy.

RESUMEN / SUMMARY: - IMPORTANCE Nonfunctioning pancreatic neuroendocrine tumors (NF-PanNETs) are often indolent neoplasms without lymph node (LN) metastasis at diagnosis. Therefore, in patients with low risk of LN metastasis, the extent of surgery and lymphadenectomy could be limited and follow-up adjusted to the very low risk of relapse. OBJECTIVE To construct a predicting model to assess the risk of pN+ prior to surgical resection for NF-PanNETs using preoperative retrievable variables. DESIGN Retrospective review using multiple logistic regression analysis to construct predictive model of pN+ based on preoperatively available data. SETTING The combined prospective databases of the Surgical Departments of the University of Verona, Verona, Italy, and Beaujon Hospital, Clichy, France, were queried for clinical and pathological data. PARTICIPANTS All patients with resected (R0 or R1), pathologically confirmed NF-PanNETs between January 1, 1993 and December 31, 2009. MAIN OUTCOME AND MEASURE Risk of lymph node metastases in patients with pancreatic neuroendocrine tumors. RESULTS Among 181 patients, nodal metastases were reported in 55 patients (30%) and were associated with decreased 5-year disease-free survival (70% vs 97%, P < .001). Multivariable analysis showed that independent factors associated with nodal metastasis were radiological nodal status (rN) (odds ratio [OR], 5.58; P < .001) and tumor grade (NET-G2 vs NET-G1: OR, 4.87; P < .001) (first model). When the tumor grade was excluded, rN (OR, 4.73; P = .001) and radiological tumor size larger than 4 cm (OR, 2.67; P = .03) were independent predictors of nodal metastasis (second model). The area under the receiver operating characteristic curve for the first and second models were 80% and 74%, respectively. CONCLUSIONS AND RELEVANCE Patients with NF-PanNET-G1 have a very low risk of

pN+ in the absence of radiological signs of node involvement. When preoperative grading assessment is not achieved, the radiological size of the lesion is a powerful alternative predictor of pN+. The risk of pathological nodal involvement in patients with NF-PanNETs can be accurately estimated by a clinical predictive model.

[305]

TÍTULO / TITLE: - An integrated transcriptome and epigenome analysis identifies a novel candidate gene for pancreatic cancer.

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

REVISTA / JOURNAL: - BMC Med Genomics. 2013 Sep 22;6(1):33.

●● Enlace al texto completo (gratis o de pago) [1186/1755-8794-6-33](#)

AUTORES / AUTHORS: - Jia J; Parikh H; Xiao W; Hoskins JW; Pflücke H; Liu X; Collins I; Zhou W; Wang Z; Powell J; Thorgeirsson SS; Rudloff U; Petersen GM; Amundadottir LT

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is a highly lethal cancer with limited diagnostic and therapeutic modalities. METHODS: To begin to explore the genomic landscape of pancreatic cancer, we used massively parallel sequencing to catalog and compare transcribed regions and potential regulatory elements in two human cell lines derived from normal and cancerous pancreas. RESULTS: By RNA-sequencing, we identified 2,146 differentially expressed genes in these cell lines that were enriched in cancer related pathways and biological processes that include cell adhesion, growth factor and receptor activity, signaling, transcription and differentiation. Our high throughput Chromatin immunoprecipitation (ChIP) sequence analysis furthermore identified over 100,000 regions enriched in epigenetic marks, showing either positive (H3K4me1, H3K4me3, RNA Pol II) or negative (H3K27me3) correlation with gene expression. Notably, an overall enrichment of RNA Pol II binding and depletion of H3K27me3 binding were seen in the cancer derived cell line as compared to the normal derived cell line. By selecting genes for further assessment based on this difference, we confirmed enhanced expression of aldehyde dehydrogenase 1^α3 (ALDH1A3) in two larger sets of pancreatic cancer cell lines and in tumor tissues as compared to normal derived tissues. CONCLUSIONS: As aldehyde dehydrogenase (ALDH) activity is a key feature of cancer stem cells, our results indicate that a member of the ALDH superfamily, ALDH1A3, may be upregulated in pancreatic cancer, where it could mark pancreatic cancer stem cells.

[306]

TÍTULO / TITLE: - Correlation between B7-H3 expression and matrix metalloproteinases 2 expression in pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Cell Int. 2013 Aug 16;13(1):81. doi: 10.1186/1475-2867-13-81.

●● Enlace al texto completo (gratis o de pago) [1186/1475-2867-13-81](#)

AUTORES / AUTHORS: - Xu L; Ding X; Tan H; Qian J

INSTITUCIÓN / INSTITUTION: - Department of Hepatopancreatobiliary Surgery, Subei People's Hospital, Yangzhou, Jiangsu 225000, China. jianjunqian99@163.com.

RESUMEN / SUMMARY: - BACKGROUND: B7-H3 and matrix metalloproteinases 2 (MMP-2) are reported highly expressed in malignant tumor, we investigate the relationship between B7-H3 expression and MMP-2 on malignant behavior and prognosis predictable value in pancreatic cancer. METHODS: We tested the expressions of B7-H3 and MMP-2 protein in 45 pancreatic surgical resected cancer samples; meanwhile, the clinicopathological data of enrolled patients were obtained for correlation analysis to obtain their relationship with pancreatic cancer progress. RESULTS: The expression of B7-H3 was up-regulated with infiltrating depth, lymph node metastasis and TNM stage ($P < 0.01$). Positive expression rate of MMP-2 in pancreatic cancer tissues was 44.35%, whereas negative in normal pancreatic tissues. Multivariate analysis of Logistic regression showed B7-H3 and MMP-2 expressions were hazardous makers correlated with infiltrating depth ($P < 0.05$). CONCLUSION: Our study showed combined detections of B7-H3 and MMP2 protein expression could identify patients at high risk in disease recurrence and prognosis more efficiently.

[307]

TÍTULO / TITLE: - Autoantibodies to Ezrin are an early sign of pancreatic cancer in humans and in genetically engineered mouse models.

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

REVISTA / JOURNAL: - J Hematol Oncol. 2013 Sep 6;6(1):67.

●● Enlace al texto completo (gratis o de pago) [1186/1756-8722-6-67](https://doi.org/10.1186/1756-8722-6-67)

AUTORES / AUTHORS: - Capello M; Cappello P; Linty FC; Chiarle R; Sperduti I; Novarino A; Salacone P; Mandili G; Naccarati A; Sacerdote C; Beghelli S; Bersani S; Barbi S; Bassi C; Scarpa A; Nistico P; Giovarelli M; Vineis P; Milella M; Novelli F

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic Ductal Adenocarcinoma (PDAC) is a highly aggressive malignancy with only a 5% 5-year survival rate. Reliable biomarkers for early detection are still lacking. The goals of this study were (a) to identify early humoral responses in genetically engineered mice (GEM) spontaneously developing PDAC; and (b) to test their diagnostic/predictive value in newly diagnosed PDAC patients and in prediagnostic sera. Methods and results The serum reactivity of GEM from inception to invasive cancer, and in resectable or advanced human PDAC was tested by two-dimensional electrophoresis Western blot against proteins from murine and human PDAC cell lines, respectively. A common mouse-to-human autoantibody signature, directed against six antigens identified by MALDI-TOF mass spectrometry, was determined. Of the six antigens, Ezrin displayed the highest frequency of autoantibodies in GEM with early disease and in PDAC patients with resectable disease. The diagnostic value of Ezrin-autoantibodies to discriminate PDAC from controls was further shown by ELISA and ROC analyses ($P < 0.0001$). This observation

was confirmed in prediagnostic sera from the EPIC prospective study in patients who eventually developed PDAC (with a mean time lag of 61.2 months between blood drawing and PDAC diagnosis). A combination of Ezrin-autoantibodies with CA19.9 serum levels and phosphorylated alpha-Enolase autoantibodies showed an overall diagnostic accuracy of 0.96 +/- 0.02. CONCLUSIONS: Autoantibodies against Ezrin are induced early in PDAC and their combination with other serological markers may provide a predictive and diagnostic signature.

[308]

TÍTULO / TITLE: - Vitamin E delta-Tocotrienol Prolongs Survival in the LSL-KrasG12D/+;LSL-Trp53R172H/+;Pdx-1-Cre (KPC) Transgenic Mouse Model of Pancreatic Cancer.

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

REVISTA / JOURNAL: - Cancer Prev Res (Phila). 2013 Oct;6(10):1074-1083. Epub 2013 Aug 20.

●● Enlace al texto completo (gratis o de pago) [1158/1940-6207.CAPR-13-0157](#)

AUTORES / AUTHORS: - Husain K; Centeno BA; Chen DT; Hingorani SR; Sebt SM; Malafa MP

INSTITUCIÓN / INSTITUTION: - Department of Gastrointestinal Oncology, Moffitt Cancer Center, 12902 Magnolia Drive, Tampa, FL 33612. mokenge.malafa@moffitt.org.

RESUMEN / SUMMARY: - Previous work has shown that vitamin E delta-tocotrienol (VEDT) prolongs survival and delays progression of pancreatic cancer in the LSL-KrasG12D/+;Pdx-1-Cre mouse model of pancreatic cancer. However, the effect of VEDT alone or in combination with gemcitabine in the more aggressive LSL-KrasG12D/+;LSL-Trp53R172H/+;Pdx-1-Cre (KPC) mouse model is unknown. Here, we studied the effects of VEDT and the combination of VEDT and gemcitabine in the KPC mice. KPC mice were randomized into four groups: (i) vehicle [olive oil, 1.0 mL/kg per os twice a day and PBS 1.0 mL/kg intraperitoneally (i.p.) twice a week], (ii) gemcitabine (100 mg/kg i.p. twice a week), (iii) VEDT (200 mg/kg per os twice a day), and (iv) gemcitabine + VEDT. Mice received treatment until they displayed symptoms of impending death from pancreatic cancer, at which point animals were euthanized. At 16 weeks, survival was 10% in the vehicle group, 30% in the gemcitabine group, 70% in the VEDT group (P < 0.01), and 90% in the VEDT combined with gemcitabine group (P < 0.05). VEDT alone and combined with gemcitabine resulted in reversal of epithelial-to-mesenchymal transition in tumors. Biomarkers of apoptosis (plasma CK18), PARP1 cleavage, and Bax expression were more greatly induced in tumors subjected to combined treatment versus individual treatment. Combined treatment induced cell-cycle inhibitors (p27Kip1 and p21Cip1) and inhibited VEGF, vascularity (CD31), and oncogenic signaling (pAKT, pMEK, and pERK) greater than individual drugs. No significant differences in body weight gain between drug treatment and control mice were observed. These

results strongly support further investigation of VEDT alone and in combination with gemcitabine for pancreatic cancer prevention and treatment. Cancer Prev Res; 6(10); 1074-83. ©2013 AACR.

[309]

TÍTULO / TITLE: - Micro-Positron Emission Tomography/Contrast-Enhanced Computed Tomography Imaging of Orthotopic Pancreatic Tumor-Bearing Mice Using the alphavbeta3 Integrin Tracer 64Cu-Labeled Cyclam-RAFT-c(-RGDfK-)-4.

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

REVISTA / JOURNAL: - Mol Imaging. 2013 Sep 1;12(6):376-87.

AUTORES / AUTHORS: - Aung W; Jin ZH; Furukawa T; Claron M; Boturyn D; Sogawa C; Tsuji AB; Wakizaka H; Fukumura T; Fujibayashi Y; Dumy P; Saga T

RESUMEN / SUMMARY: - AbstractThe purpose of this study was to develop a clinically relevant orthotopic xenotransplantation model of pancreatic cancer and to perform a preclinical evaluation of a new positron emission tomography (PET) imaging probe, 64Cu-labeled cyclam-RAFT-c(-RGDfK-)-4 peptide (64Cu-RAFT-RGD), using this model. Varying degrees of alphavbeta3 integrin expression in several human pancreatic cancer cell lines were examined by flow cytometry and Western blotting. The cell line BxPC-3, which is stably transfected with a red fluorescence protein (RFP), was used for surgical orthotopic implantation. Orthotopic xenograft was established in the pancreas of recipient nude mice. An in vivo probe biodistribution and receptor blocking study, preclinical PET imaging coregistered with contrast-enhanced computed tomography (CECT) comparing 64Cu-RAFT-RGD and 18F-fluoro-2-deoxy-d-glucose (18F-FDG) accumulation in tumor, postimaging autoradiography, and histologic and immunohistochemical examinations were done. Biodistribution evaluation with a blocking study confirmed that efficient binding of probe to tumor is highly alphavbeta3 integrin specific. 64Cu-RAFT-RGD PET combined with CECT provided for precise and easy detection of cancer lesions. Autoradiography, histologic, and immunohistochemical examinations confirmed the accumulation of 64Cu-RAFT-RGD in tumor versus nontumor tissues. In comparative PET studies, 64Cu-RAFT-RGD accumulation provided better tumor contrast to background than 18F-FDG. Our results suggest that 64Cu-RAFT-RGD PET imaging is potentially applicable for the diagnosis of alphavbeta3 integrin-expressing pancreatic tumors.

[310]

TÍTULO / TITLE: - Role of magnetic resonance cholangiopancreatography in diagnosing choledochal cysts: Case series and review.

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

REVISTA / JOURNAL: - World J Radiol. 2013 Aug 28;5(8):304-12. doi: 10.4329/wjr.v5.i8.304.

●● Enlace al texto completo (gratis o de pago) [4329/wjr.v5.i8.304](#)

AUTORES / AUTHORS: - Sacher VY; Davis JS; Sleeman D; Casillas J

INSTITUCIÓN / INSTITUTION: - Vikas Y Sacher, James S Davis, Danny Sleeman, Department of Surgery, University of Miami, Miami, FL 33136, United States.

RESUMEN / SUMMARY: - AIM: To determine the merits of magnetic resonance cholangiopancreatography (MRCP) as the primary diagnostic test for choledochal cysts (CC's). METHODS: Between 2009 and 2012, patients who underwent MRCP for perioperative diagnosis were identified. Demographic information, clinical characteristics, and radiographic findings were recorded. MRCP results were compared with intraoperative findings. A PubMed search identified studies published between 1996-2012, employing MRCP as the primary preoperative imaging and comparing results with either endoscopic retrograde cholangiopancreatography (ERCP) or operative findings. Detection rates for CC's and abnormal pancreaticobiliary junction (APBJ) were calculated. In addition detection rates for clinically related biliary pathology like choledocholithiasis and cholangiocarcinomas in patients diagnosed with CC's were also evaluated. RESULTS: Eight patients were identified with CC's. Six patients out of them had type IV CC's, 1 had type I and 1 had a new variant of choledochal cyst with confluent dilatation of the common bile duct (CBD) and cystic duct. Seven patients had an APBJ and 3 of those had a long common-channel. Gallstones were found in 2 patients, 1 had a CBD stone, and 1 pancreatic-duct stone was also detected. In all cases, MRCP successfully identified the type of CC's, as well as APBJ with ductal stones. From analyzing the literature, we found that MRCP has 96%-100% detection rate for CC's. Additionally, we found that the range for sensitivity, specificity, and diagnostic accuracy was 53%-100%, 90%-100% and 56%-100% in diagnosing APBJ. MRCP's detection rate was 100% for choledocholithiasis and 87% for cholangiocarcinomas with concurrent CC's. CONCLUSION: After initial ultrasound and computed tomography scan, MRCP should be the next diagnostic test in both adult and pediatric patients. ERCP should be reserved for patients where therapeutic intervention is needed.

[311]

TÍTULO / TITLE: - A large cystic pancreatic mass in a 45-year-old female.

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

REVISTA / JOURNAL: - Oncology (Williston Park). 2013 Jul;27(7):669, 674.

AUTORES / AUTHORS: - Lammers A; McManus MC; Purcell WT

INSTITUCIÓN / INSTITUTION: - Department of Medicine, University of Colorado School of Medicine, University of Colorado Cancer Center, Aurora, Colorado, USA.

[312]

TÍTULO / TITLE: - Targeting cancer-related inflammation: Chinese herbal medicine inhibits epithelial-to-mesenchymal transition in pancreatic cancer.

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

REVISTA / JOURNAL: - PLoS One. 2013 Jul 29;8(7):e70334. doi: 10.1371/journal.pone.0070334. Print 2013.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0070334](https://doi.org/10.1371/journal.pone.0070334)

AUTORES / AUTHORS: - Zhang J; Wang P; Ouyang H; Yin J; Liu A; Ma C; Liu L

INSTITUCIÓN / INSTITUTION: - Department of Integrative Oncology, Fudan University Shanghai Cancer Center, Shanghai, China.

RESUMEN / SUMMARY: - Pancreatic cancer is an almost universally fatal disease resulting from early invasion of adjacent structures and metastasis and the lack of an effective treatment modality. Our previous studies have shown that Qingyihuaji Formula (QYHJ), a seven-herb Chinese medicine formula, had significant anti-cancer effects in pancreatic cancer. Here, we examined the effects of QYHJ on pancreatic cancer cell invasion and metastasis and the potential associated mechanism(s). We found that QYHJ inhibited both tumor growth and metastasis in nude mice with human pancreatic cancer cell xenografts. Further study indicated that QYHJ inhibited epithelial-to-mesenchymal transition (EMT), which is characterized by increased E-cadherin expression and decreased vimentin, N-cadherin and Slug expression. Interleukin 6 (IL-6), a pro-inflammatory cytokine produced mainly by macrophages, could promote cancer cell EMT and invasion. In contrast, treatment with QYHJ inhibited cancer-related inflammation in tumors by decreasing infiltration of tumor-associated macrophages and IL-6 production, thus preventing cell invasion and metastasis. These results suggested that the Chinese herbal medicine QYHJ could inhibit pancreatic cancer cell invasion and metastasis in part by reversing tumor-supporting inflammation.

[313]

TÍTULO / TITLE: - Soap puts pancreatic cancer in spotlight.

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

REVISTA / JOURNAL: - Nurs Stand. 2013 Sep 11;28(2):9. doi: 10.7748/ns2013.09.28.2.9.s12.

●● Enlace al texto completo (gratis o de pago) [7748/ns2013.09.28.2.9.s12](https://doi.org/10.7748/ns2013.09.28.2.9.s12)

RESUMEN / SUMMARY: - Millions of Coronation Street viewers last week watched character Hayley Cropper (pictured alongside husband Roy) being told her pancreatic cancer tumour is inoperable and that she only has up to a year to live.

[314]

TÍTULO / TITLE: - IL-1alpha Expression in Pancreatic Ductal Adenocarcinoma Affects the Tumor Cell Migration and Is Regulated by the p38MAPK Signaling Pathway.

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

REVISTA / JOURNAL: - PLoS One. 2013;8(8):e70874. doi: 10.1371/journal.pone.0070874.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0070874](https://doi.org/10.1371/journal.pone.0070874)

AUTORES / AUTHORS: - Tjomsland V; Bojmar L; Sandstrom P; Bratthall C; Messmer D; Spangeus A; Larsson M

INSTITUCIÓN / INSTITUTION: - Molecular Virology, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden.

RESUMEN / SUMMARY: - The interplay between the tumor cells and the surrounding stroma creates inflammation, which promotes tumor growth and spread. The inflammation is a hallmark for pancreatic adenocarcinoma (PDAC) and is to high extent driven by IL-1alpha. IL-1alpha is expressed and secreted by the tumor cells and exerting its effect on the stroma, i.e. cancer associated fibroblasts (CAF), which in turn produce massive amount of inflammatory and immune regulatory factors. IL-1 induces activation of transcription factors such as nuclear factor-kappabeta (NF-kappabeta), but also activator protein 1 (AP-1) via the small G-protein Ras. Dysregulation of Ras pathways are common in cancer as this oncogene is the most frequently mutated in many cancers. In contrast, the signaling events leading up to the expression of IL-1alpha by tumor cells are not well elucidated. Our aim was to examine the signaling cascade involved in the induction of IL-1alpha expression in PDAC. We found p38MAPK, activated by the K-Ras signaling pathway, to be involved in the expression of IL-1alpha by PDAC as blocking this pathway decreased both the gene and protein expression of IL-1alpha. Blockage of the P38MAPK signaling in PDAC also dampened the ability of the tumor cell to induce inflammation in CAFs. In addition, the IL-1alpha autocrine signaling regulated the migratory capacity of PDAC cells. Taken together, the blockage of signaling pathways leading to IL-1alpha expression and/or neutralization of IL-1alpha in the PDAC microenvironment should be taken into consideration as possible treatment or complement to existing treatment of this cancer.

[315]

TÍTULO / TITLE: - MiR-130b Is a Prognostic Marker and Inhibits Cell Proliferation and Invasion in Pancreatic Cancer through Targeting STAT3.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 10;8(9):e73803. doi: 10.1371/journal.pone.0073803.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0073803](https://doi.org/10.1371/journal.pone.0073803)

AUTORES / AUTHORS: - Zhao G; Zhang JG; Shi Y; Qin Q; Liu Y; Wang B; Tian K; Deng SC; Li X; Zhu S; Gong Q; Niu Y; Wang CY

INSTITUCIÓN / INSTITUTION: - Pancreatic Disease Institute, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

RESUMEN / SUMMARY: - Accumulating evidence indicates that microRNAs (miRNAs) are aberrantly expressed in human cancer and contribute to the tumorigenesis, but their roles in pancreatic cancer are still largely unknown. In this study, our data showed that miR-130b was significantly downregulated in 52 pairs of pancreatic cancer tissues and five cell lines. Furthermore, the deregulated miR-130b was correlated with worse

prognosis, increased tumor size, late TNM stage, lymphatic invasion and distant metastasis. Multivariate analysis showed that miR-130b expression was a significant and independent prognostic predictor for pancreatic cancer patients. Functional studies indicated that the overexpression of miR-130b dramatically suppressed the proliferation of pancreatic cancer cells both in vitro and in vivo, which could be attributed to the induction of apoptosis and cell cycle arrest at S phase. Meanwhile, an overexpressed miR-130b remarkably inhibited the invasive ability of pancreatic cancer cells. Moreover, the dual luciferase assay revealed that STAT3 was directly targeted by miR-130b, which was further confirmed by the inverse expression of miR-130b and STAT3 in pancreatic cancer samples. Our findings suggested that miR-130b might have a considerable potential in prognosis identification and application of therapy for pancreatic cancer.

[316]

TÍTULO / TITLE: - Pancreatic glucagonoma metastasising to the right ovary five years after initial surgery: a case report.

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

REVISTA / JOURNAL: - JOP. 2013 Sep 10;14(5):510-4. doi: 10.6092/1590-8577/1622.

AUTORES / AUTHORS: - Watt DG; Pandanaboyana S; Herrington CS; Tait IS

INSTITUCIÓN / INSTITUTION: - General Surgery, Ninewells Hospital and Medical School. Dundee, Scotland, United Kingdom. davidwatt1@nhs.net.

RESUMEN / SUMMARY: - CONTEXT: Glucagonomas of the pancreas are neuroendocrine tumours (NETs) that arise from well-differentiated neuroendocrine cells within the pancreatic islets. They are considered to be aggressive NETs and often have metastases at initial presentation. In contrast localised glucagonoma without metastatic spread may have prolonged disease free survival with radical resectional surgery. CASE REPORT: The authors present a case of a glucagonoma that initially presented with classical necrolytic migratory erythema and a large solitary mass in the body and tail of the pancreas that was surgically resected. Five years after surgery the patient presented with increased serum glucagon levels and a mass in the right ovary. Pathology of the resected ovary after oophorectomy identified this as an isolated metastatic glucagonoma. CONCLUSION: Glucagonoma is a rare pancreatic NET that has significant malignant potential. This is the first case of a pancreatic glucagonoma metastasising to the ovary 5 years after radical distal pancreatectomy.

[317]

TÍTULO / TITLE: - Superficial Necrolytic Dermatitis in a Dog With an Insulin-Producing Pancreatic Islet Cell Carcinoma.

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

REVISTA / JOURNAL: - Vet Pathol. 2013 Sep 10.

●● Enlace al texto completo (gratis o de pago) [1177/0300985813503567](https://doi.org/10.1177/0300985813503567)

AUTORES / AUTHORS: - Isidoro-Ayza M; Lloret A; Bardagi M; Ferrer L; Martinez J

INSTITUCIÓN / INSTITUTION: - Veterinary School, Universitat Autònoma de Barcelona, Barcelona, España.

RESUMEN / SUMMARY: - A 10-year-old dog presented with convulsive crisis and symmetrical hyperkeratotic cutaneous lesions affecting the abdomen, inguinal area, eyelids, muzzles, both pinnae, and all the paw pads. Hypoglycemia and hyperinsulinemia were the main biochemical findings. A mass 2 cm in diameter was detected within the left pancreatic lobe by ultrasonography. It was surgically removed and histologically and immunohistochemically diagnosed as an insulin-producing pancreatic islet cell carcinoma. The animal was eventually euthanized due to lack of clinical improvement. At necropsy, metastatic nodules were observed in the pancreatic lymph nodes and liver. Histopathological findings of cutaneous lesions were highly suggestive of superficial necrolytic dermatitis and were interpreted as a paraneoplastic syndrome derived from the islet cell carcinoma. To the authors' knowledge, this is the first report of superficial necrolytic dermatitis associated with an insulin-producing pancreatic neuroendocrine carcinoma in dogs.

[318]

TÍTULO / TITLE: - MicroRNAs as diagnostic markers for pancreatic ductal adenocarcinoma and its precursor, pancreatic intraepithelial neoplasm.

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

REVISTA / JOURNAL: - Cancer Genet. 2013 Jun;206(6):217-21. doi: 10.1016/j.cancergen.2013.05.020. Epub 2013 Aug 9.

●● Enlace al texto completo (gratis o de pago) [1016/j.cancergen.2013.05.020](https://doi.org/10.1016/j.cancergen.2013.05.020)

AUTORES / AUTHORS: - Xue Y; Abou Tayoun AN; Abo KM; Pipas JM; Gordon SR; Gardner TB; Barth RJ Jr; Suriawinata AA; Tsongalis GJ

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Geisel School of Medicine at Dartmouth, Hanover, NH -and- Dartmouth Hitchcock Medical Center and Norris Cotton Cancer Center, Lebanon, NH.

RESUMEN / SUMMARY: - Since the discovery of small non-coding RNAs, the analysis of microRNA (miRNA) expression patterns in human cancer have provided new insights into cancer biology. Evidence suggests that deregulated miRNA expression is associated with pancreatic cancer development. In this study, we analyzed the expression of several miRNAs in different types of pancreatic disease to determine if miRNA expression could aid in the diagnosis of pancreatic ductal adenocarcinoma (PDAC) and its precursor, pancreatic intraepithelial neoplasm (PanIN). Pancreatic resection specimens were selected, which included PDAC (n = 16), benign pancreatic parenchyma from corresponding carcinoma cases (n = 16), chronic pancreatitis (n = 4), normal pancreatic parenchyma (n = 5), and PanIN (n = 5). The expression levels of five miRNA (miR-148^a, miR-217, miR-21, miR-196^a, and miR-10b) were assessed by

quantitative real-time reverse transcription-polymerase chain reaction (qRT-PCR) assays. Our data demonstrate that compared to the normal pancreatic parenchyma, miR-148^a and miR-217 expression levels were down-regulated in PanIN, particularly in PanIN II-III and PDAC, whereas the level of miR-196 was significantly up-regulated in PDAC and its precursor, PanIN II-III. In addition, we observed that miR-21 was significantly overexpressed in PDAC, and miR-10b was highly expressed in PanIN II-III. Our study demonstrates that certain miRNAs, especially miR-148^a, miR-217, and miR-196^a, are significantly deregulated in PDAC, including in the early stage of PDAC. These markers can potentially be used as diagnostic markers to distinguish PDAC and its precursor from benign lesions.

[319]

TÍTULO / TITLE: - Pituitary Metastasis of Pancreatic Origin in a Dog Presenting with Acute-Onset Blindness.

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

REVISTA / JOURNAL: - J Am Anim Hosp Assoc. 2013 Sep 19.

●● Enlace al texto completo (gratis o de pago) [5326/JAAHA-MS-5926](#)

AUTORES / AUTHORS: - Gutierrez-Quintana R; Carrera I; Dobromylskyj M; Patterson-Kane J; Ortega M; Wessmann A

INSTITUCIÓN / INSTITUTION: - Small Animal Clinical Sciences, College of Medical, Veterinary & Life Sciences, University of Glasgow, Glasgow, UK; Section of Diagnostic Imaging, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland (I.C.).

RESUMEN / SUMMARY: - Pituitary metastases have rarely been recorded in dogs, and to date, none of those reported have been of pancreatic origin. MRI findings are available for only one of those cases. Herein the authors present an 11 yr old English springer spaniel diagnosed with pituitary metastasis of pancreatic origin with a 24 hr history of blindness and only a single lesion on MRI. Neurologic and ophthalmologic examinations localized the lesion to the optic nerves, optic tracts, or optic chiasm. MRI showed a single lesion characterized by a well-circumscribed pituitary mass with extrasellar extension, causing compression of the optic chiasm. Signal intensity was unusual as enhancement could not be appreciated after contrast administration. The dog was euthanized without further diagnostic tests. Histopathologic examination revealed a poorly differentiated exocrine pancreatic carcinoma with widespread metastasis involving the pituitary gland. To the authors' knowledge, this is the first such case reported in a dog. Pituitary metastases should be included as a differential diagnosis for dogs presenting with acute-onset blindness and for single brain masses affecting the pituitary gland.

[320]

TÍTULO / TITLE: - Characteristics and outcomes of adenosquamous carcinoma of the pancreas.

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

REVISTA / JOURNAL: - Gastrointest Cancer Res. 2013 May;6(3):75-9.

AUTORES / AUTHORS: - Simone CG; Zuluaga Toro T; Chan E; Feely MM; Trevino JG; George TJ Jr

INSTITUCIÓN / INSTITUTION: - Division of Hematology and Oncology Department of Medicine.

RESUMEN / SUMMARY: - BACKGROUND: Adenosquamous carcinoma of the pancreas (ASCAP) is a rare histologic type of pancreatic carcinoma that constitutes 1% to 4% of all pancreatic exocrine malignancies. It has a clinical presentation similar to that of adenocarcinoma of the pancreas (ACP), but may have a worse overall prognosis, with most patients surviving for less than 2 years. METHODS: This was an institutional, retrospective, cohort analysis of 237 patients who underwent resection of pancreatic cancer with curative intent. RESULTS: Of the 237 cases examined, we identified 7 (2.9%) with histologically confirmed ASCAP. Demographics, comorbidities, risk factors, presenting symptoms, survival data, tumor characteristics, and types of treatment for each patient were included in the analysis. Risk factors for development of ASCAP were not conclusive. Although human papilloma virus (HPV) has been implicated in other squamous cell cancers, in our cohort, its involvement in ASCAP was 0%. Presurgical fine-needle aspiration failed to identify the invasive squamous cell component in all cases. In this cohort analysis, overall survival ranged from 3 to 25 months, with 2 patients surviving more than 20 months after surgical resection. With a median follow-up of 2.9 years, our data demonstrate a trend to worse median overall survival for ASCAP than for ACP (8.2 vs. 20.4 months; P = .23), with a limited number of long-term survivors. CONCLUSIONS: Although recommended, adjuvant treatment was inconsistently provided for patients in this ASCAP cohort. Published data show variability in overall survival, but our findings support that surgical resection is one of the few options for control of this rare, poorly understood pancreatic malignancy. Further research is necessary to define risk factors and adjuvant and neoadjuvant treatments, to help improve patient outcomes.

[321]

TÍTULO / TITLE: - Renal cell carcinoma with concomitant solid pseudopapillary tumor of the pancreas: A case report.

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

REVISTA / JOURNAL: - Int J Surg Case Rep. 2013;4(10):828-30. doi: 10.1016/j.ijscr.2013.06.011. Epub 2013 Jul 16.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.ijscr.2013.06.011](#)

AUTORES / AUTHORS: - Atilgan D; Kilic S; Kayaoglu HA; Koseoglu RD

INSTITUCIÓN / INSTITUTION: - Gaziosmanpasa University, Faculty of Medicine, Department of Urology, Tokat, Turkey. Electronic address: datilgan@msn.com.

RESUMEN / SUMMARY: - INTRODUCTION: Solid pseudopapillary tumor (SPT) of pancreas is an unusual low-grade malignant epithelial tumor that usually occurs in young women and can be treated with surgical resection. Renal cell carcinoma (RCC) is the most common solid lesion of the kidney and primarily a disease of the elderly patient. PRESENTATION OF CASE: In this article we present a case of RCC with concomitant SPT of the pancreas who was treated successfully with a radical nephrectomy and distal pancreatectomy. DISCUSSION: RCC with concomitant SPT may associated in beta-catenin gene mutation. But no prior reports have described RCC with concomitant SPT of the pancreas in the same patient. CONCLUSION: To the best of our knowledge, this is the first report of RCC with concomitant SPT of the pancreas in the same patient.

[322]

TÍTULO / TITLE: - An extremely rare case of pancreatic cancer presenting with leptomeningeal carcinomatosis and synchronous intraparenchymal brain metastasis.

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

REVISTA / JOURNAL: - Gastrointest Cancer Res. 2013 May;6(3):90-2.

AUTORES / AUTHORS: - Rao R; Sadashiv SK; Goday S; Monga D

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine West Penn Allegheny Health System Pittsburgh, PA.

[323]

TÍTULO / TITLE: - Uncomplicated spontaneous rupture of pancreatic pseudocyst into stomach: A case report.

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

REVISTA / JOURNAL: - World J Gastrointest Endosc. 2013 Sep 16;5(9):461-4. doi: 10.4253/wjge.v5.i9.461.

●● [Enlace al texto completo \(gratis o de pago\) 4253/wjge.v5.i9.461](#)

AUTORES / AUTHORS: - Somani PO; Jain SS; Shah DK; Khot AA; Rathi PM

INSTITUCIÓN / INSTITUTION: - Piyush O Somani, Samit S Jain, Dharmesh K Shah, Amol A Khot, Pravin M Rathi, Department of Gastroenterology, Topiwala National Medical College, Bai Yamunabai Laxman Nair Hospital, Mumbai 400008, India.

RESUMEN / SUMMARY: - Pseudocysts of the pancreas are not rare, but spontaneous perforation and/or fistulization occurs in fewer than 3% of these pseudocysts. Perforation into the free peritoneal cavity, stomach, duodenum, colon, portal vein, pleural cavity and through the abdominal wall has been reported. Spontaneous rupture of the pancreatic pseudocyst into the surrounding hollow viscera is rare and, may be associated with life-threatening bleeding. Such cases require emergency surgical intervention. Uncomplicated rupture of pseudocyst is an even rarer occurrence. We present a case of spontaneous resolution of a pancreatic pseudocyst

with gastric connection without bleeding. A 67-year-old women with a large pancreatic pseudocyst resulting from a complication of chronic pancreatitis was referred to our institution. During hospital stay, there was sudden decrease in the size of epigastric lump. Repeat computed tomography (CT) revealed that the size of the pseudocyst had decreased significantly; however, gas was observed in stomach and pseudocyst along with rent between lesser curvature of stomach and pseudocyst suggestive of spontaneous cystogastric fistula. The fistula tract occluded spontaneously and the patient recovered without any complication or need for surgical treatment. After 5 wk, follow up CT revealed complete resolution of pseudocyst. Esophagogastroduodenoscopy revealed that the orifice was completely occluded with ulcer at the site of previous fistulous opening.

[324]

TÍTULO / TITLE: - The presence of tumour-associated lymphocytes confers a good prognosis in pancreatic ductal adenocarcinoma: an immunohistochemical study of tissue microarrays.

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

REVISTA / JOURNAL: - BMC Cancer. 2013 Sep 24;13(1):436.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-436](#)

AUTORES / AUTHORS: - Tewari N; Arora A; Madhusudan S; Ilyas M; Lobo DN

RESUMEN / SUMMARY: - BACKGROUND: Tumour-associated lymphocytes (TALs) have been linked with good prognosis in several solid tumours. This study aimed to evaluate the prognostic significance of CD3, CD8 and CD20 positive lymphocytes in pancreatic ductal adenocarcinoma. METHODS: After histological re-evaluation of the tumours of 81 patients who underwent surgical resection for exclusively pancreatic ductal adenocarcinoma, tissue micro-arrays (TMA) were constructed and immunohistochemistry was performed for CD3, CD8 and CD20. The number of lymphocytes within specific tumour compartments (i.e. stromal and intratumoural) was quantified. X-tile software (Yale School of Medicine, CT, USA) was used to stratify patients into 'high' and 'low' for each of the lymphocytes stained and their association with survival. Receiver operating curves (ROC) were constructed to evaluate the association between the TALs, alone and in combination, with clinicopathological features. RESULTS: CD3 and CD8 positive lymphocytes were associated with grade of tumour differentiation. The presence of intratumoural CD3 positive cells was associated with improved survival ($p = 0.028$), and intratumoural and stromal CD3 in combination also correlated with improved survival ($p = 0.043$). When CD20 positive lymphocyte levels were high, survival improved ($p = 0.029$) and similar results were seen for CD20 in combination with intratumoural CD3 ($p = 0.001$) and stromal CD8 ($p = 0.013$). CONCLUSIONS: This study has shown a correlation between the presence of TALs and survival in pancreatic ductal adenocarcinoma.

[325]

TÍTULO / TITLE: - Optimal chemotherapy dosing in a bilateral lower extremities amputee with metastatic pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Gastrointest Cancer Res. 2013 May;6(3):93-4.

AUTORES / AUTHORS: - Owen D; O'Reilly EM; Ang C; Ma J; Do RK; Abou-Alfa GK

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

[326]

TÍTULO / TITLE: - Histology combined with cytology by endoscopic ultrasound-guided fine needle aspiration for the diagnosis of solid pancreatic mass and intra-abdominal lymphadenopathy.

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

REVISTA / JOURNAL: - Gut Liver. 2013 Sep;7(5):605-10. doi: 10.5009/gnl.2013.7.5.605. Epub 2013 Jun 11.

●● Enlace al texto completo (gratis o de pago) [5009/gnl.2013.7.5.605](#)

AUTORES / AUTHORS: - Kim TH; Choi KH; Song HS; Kim JW; Jeon BJ

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Wonkwang University Hospital, Wonkwang University School of Medicine, Iksan, Korea.

RESUMEN / SUMMARY: - BACKGROUND/AIMS: Small core biopsy samples can occasionally be obtained with conventional endoscopic ultrasonography-guided fine needle aspiration (EUS-FNA). Although most studies have focused on the cytological analysis of specimens, data regarding histological assessment is scarce. The aim of this study was to determine whether core biopsies by conventional EUS-FNA could increase the accuracy of EUS-guided sampling when combined with cytology in the absence of an on-site cytopathologist. METHODS: In the 95 consecutive patients (98 lesions) undergoing EUS-FNA of solid pancreatic masses and intra-abdominal lymphadenopathy, tissue coils from the needle were harvested for histology, and residual tissue was examined by cytology. RESULTS: Adequate samples were obtained by EUS-FNA cytology, histology, and combined cytology-histology in 91.8%, 65.3%, and 94.8% of patients, respectively. From the pancreas (n=67), adequate samples for histology were obtained by EUS-FNA in 68.7% of cases, compared with 58.0% from non-pancreatic cases (n=31), respectively (p>0.05). The overall sensitivity and accuracy of EUS-FNA was 78.0% and 81.6% for cytology alone, 63.4% and 69.4% for histology alone, and 84.1% and 86.7% for combined cytology-histology, respectively. CONCLUSIONS: Combined cytology and histology analysis for diagnosing pancreatic masses and intra-abdominal lymphadenopathy may increase the diagnostic yield of conventional EUS-FNA without on-site cytology.

[327]

TÍTULO / TITLE: - Intratumoral alpha-SMA Enhances the Prognostic Potency of CD34 Associated with Maintenance of Microvessel Integrity in Hepatocellular Carcinoma and Pancreatic Cancer.

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

REVISTA / JOURNAL: - PLoS One. 2013 Aug 5;8(8):e71189. doi: 10.1371/journal.pone.0071189. Print 2013.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0071189](#)

AUTORES / AUTHORS: - Wang WQ; Liu L; Xu HX; Luo GP; Chen T; Wu CT; Xu YF; Xu J; Liu C; Zhang B; Long J; Tang ZY; Yu XJ

INSTITUCIÓN / INSTITUTION: - Department of Pancreatic and Hepatobiliary Surgery, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University; and Pancreatic Cancer Institute, Fudan University, Shanghai, China.

RESUMEN / SUMMARY: - Microvessel density (MVD) as an angiogenesis predictor is inefficient per se in cancer prognosis. We evaluated prognostic values of combining intratumoral alpha-smooth muscle actin (alpha-SMA)-positive stromal cell density and MVD after curative resection in hypervascular hepatocellular carcinoma (HCC) and hypovascular pancreatic cancer (PC). Tissue microarrays were constructed from tumors of 305 HCC and 57 PC patients who underwent curative resection and analyzed for alpha-SMA and CD34 expression by immunostaining. Prognostic values of these two proteins and other clinicopathological features were examined. Both low alpha-SMA density and high MVD-CD34 were associated in HCC with the presence of intrahepatic metastasis and microvascular invasion, and they were related to lymph node involvement and microvascular invasion in PC ($p < 0.05$). Although CD34 alone, but not alpha-SMA, was an independent prognostic factor for overall survival and recurrence-free survival, the combination of low alpha-SMA and high CD34 was a predictor of worst prognosis for both types of tumors and had a better power to predict patient death and early recurrence ($p < 0.01$). Furthermore, the results show that distribution of most of the alpha-SMA-positive cells and vascular endothelial cells overlap, showing major colocalization on vascular walls. Poor microvessel integrity, as indicated by high MVD, together with low perivascular alpha-SMA-positive cell coverage is associated with early recurrence, unfavorable metastasis, and short survival after tumor resection. This finding highlights the significance of vascular quality in tumor progression, which provides an optimized complement to vascular quantity in prognosis of postoperative patients.

[328]

TÍTULO / TITLE: - High-Fat, High-Calorie Diet Promotes Early Pancreatic Neoplasia in the Conditional KrasG12D Mouse Model.

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

REVISTA / JOURNAL: - Cancer Prev Res (Phila). 2013 Oct;6(10):1064-1073. Epub 2013 Aug 13.

●● Enlace al texto completo (gratis o de pago) [1158/1940-6207.CAPR-13-0065](https://doi.org/10.1158/1940-6207.CAPR-13-0065)

AUTORES / AUTHORS: - Dawson DW; Hertzner K; Moro A; Donald G; Chang HH; Go VL; Pandol SJ; Lugea A; Gukovskaya AS; Li G; Hines OJ; Rozengurt E; Eibl G

INSTITUCIÓN / INSTITUTION: - Department of Surgery, David Geffen School of Medicine, University of California at Los Angeles, 10833 LeConte Avenue, 72-236 CHS, Los Angeles, CA 90095. Geibl@mednet.ucla.edu.

RESUMEN / SUMMARY: - There is epidemiologic evidence that obesity increases the risk of cancers. Several underlying mechanisms, including inflammation and insulin resistance, are proposed. However, the driving mechanisms in pancreatic cancer are poorly understood. The goal of the present study was to develop a model of diet-induced obesity and pancreatic cancer development in a state-of-the-art mouse model, which resembles important clinical features of human obesity, for example, weight gain and metabolic disturbances. Offspring of Pdx-1-Cre and LSL-KrasG12D mice were allocated to either a high-fat, high-calorie diet (HFCD; approximately 4,535 kcal/kg; 40% of calories from fats) or control diet (approximately 3,725 kcal/kg; 12% of calories from fats) for 3 months. Compared with control animals, mice fed with the HFCD significantly gained more weight and developed hyperinsulinemia, hyperglycemia, hyperleptinemia, and elevated levels of insulin-like growth factor I (IGF-I). The pancreas of HFCD-fed animals showed robust signs of inflammation with increased numbers of infiltrating inflammatory cells (macrophages and T cells), elevated levels of several cytokines and chemokines, increased stromal fibrosis, and more advanced PanIN lesions. Our results show that a diet high in fats and calories leads to obesity and metabolic disturbances similar to humans and accelerates early pancreatic neoplasia in the conditional KrasG12D mouse model. This model and findings will provide the basis for more robust studies attempting to unravel the mechanisms underlying the cancer-promoting properties of obesity, as well as to evaluate dietary- and chemopreventive strategies targeting obesity-associated pancreatic cancer development. Cancer Prev Res; 6(10); 1064-73. ©2013 AACR.

[329]

TÍTULO / TITLE: - From Acute Pancreatitis to Stage IV Pancreatic Cancer in 12 Weeks.

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

REVISTA / JOURNAL: - Case Rep Gastroenterol. 2013 Jul 13;7(2):287-92. doi: 10.1159/000354146. Print 2013 May.

●● Enlace al texto completo (gratis o de pago) [1159/000354146](https://doi.org/10.1159/000354146)

AUTORES / AUTHORS: - Enwelu C; Dutta S; Aziz F; Lenfest S

INSTITUCIÓN / INSTITUTION: - Section on Hospital Medicine, Department of Internal Medicine, Winston Salem, N.C., USA.

RESUMEN / SUMMARY: - Pancreatic cancer is well known to be an aggressive and highly malignant condition with varied ways of presentation. Pancreatic cystic neoplasms are very uncommon causes of pancreatic malignancy and can often be ignored or missed, especially in the early stages. We present the case of a 49-year-old Caucasian male with no past medical history presenting to an outside facility with sudden epigastric pain that was eventually diagnosed as acute pancreatitis. On transfer to our facility, he was eventually found to have metastatic malignant mucinous cystic pancreatic neoplasm. Barely 12 weeks after his initial presentation and following an aggressive hospital course, he passed away.

[330]

TÍTULO / TITLE: - Fine-needle aspirations of pancreatic serous cystadenomas: Improving diagnostic yield with cell blocks and alpha-inhibin immunohistochemistry.

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

REVISTA / JOURNAL: - Cancer Cytopathol. 2013 Aug 12. doi: 10.1002/cncy.21347.

●● [Enlace al texto completo \(gratis o de pago\) 1002/cncy.21347](#)

AUTORES / AUTHORS: - Salomao M; Remotti H; Allendorf JD; Poneros JM; Sethi A; Gonda TA; Saqi A

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Cell Biology, Columbia University Medical Center, New York, New York.

RESUMEN / SUMMARY: - **BACKGROUND:** The diagnosis of serous cystadenoma (SCA), a rare benign pancreatic neoplasm, can alter the management of patients with pancreatic masses. Although characteristic imaging findings and fluid chemical analysis have been described, SCAs are not always recognized preoperatively. Furthermore, scant cellular yield on fine-needle aspiration (FNA) often leads to a nondiagnostic or nonspecific benign diagnosis. alpha-Inhibin (AI), a sensitive marker for SCA, is infrequently required for diagnosis in surgical specimens due to their characteristic histologic appearance. The objective of the current study was to determine whether AI staining can improve SCA diagnosis on FNA specimens. **METHODS:** Fifteen confirmed cases of SCA with prior FNA specimens were selected for this study. FNAs were evaluated for cellularity, cellular arrangement, and cytomorphology. Resection specimens were reviewed. **RESULTS:** Of the 15 FNA cases, approximately 75% demonstrated scant cellularity (11 of 15 cases). On smears, the cells were arranged as flat sheets, corresponding to strips of cells on cell block sections. The cells were small and round to cuboidal, with clear cytoplasm; occasional plasmacytoid cells and oncocytic cells were identified. Flattened cells, corresponding to attenuated epithelial cells lining macrocysts on the resections, were also noted. Stromal fragments were present in 5 FNAs and correlated with the hyalinized stroma in the resection specimens. AI immunostaining was positive in 88% of cases (7 of 8 of cases), thereby supporting the diagnosis of SCA. **CONCLUSIONS:** The results of the current study indicate that low cellularity and bland cytology are inherent to SCAs. Performing cell

blocks and AI staining on FNA specimens is useful for establishing the diagnosis of SCA. An immunohistochemical panel including AI, chromogranin, and synaptophysin may enhance the diagnostic accuracy of pancreatic FNA specimens. Cancer (Cancer Cytopathol) 2013. © 2013 American Cancer Society.

[331]

TÍTULO / TITLE: - Validation of four candidate pancreatic cancer serological biomarkers that improve the performance of CA19.9.

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

REVISTA / JOURNAL: - BMC Cancer. 2013 Sep 3;13(1):404.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-404](#)

AUTORES / AUTHORS: - Makawita S; Dimitromanolakis A; Soosaipillai A; Soleas I; Chan A; Gallinger S; Haun RS; Blasutig IM; Diamandis EP

RESUMEN / SUMMARY: - BACKGROUND: The identification of new serum biomarkers with high sensitivity and specificity is an important priority in pancreatic cancer research. Through an extensive proteomics analysis of pancreatic cancer cell lines and pancreatic juice, we previously generated a list of candidate pancreatic cancer biomarkers. The present study details further validation of four of our previously identified candidates: regenerating islet-derived 1 beta (REG1B), syncollin (SYCN), anterior gradient homolog 2 protein (AGR2), and lysyl oxidase-like 2 (LOXL2). METHODS: The candidate biomarkers were validated using enzyme-linked immunosorbent assays in two sample sets of serum/plasma comprising a total of 432 samples (Sample Set A: pancreatic ductal adenocarcinoma (PDAC, n = 100), healthy (n = 92); Sample Set B: PDAC (n = 82), benign (n = 41), disease-free (n = 47), other cancers (n = 70)). Biomarker performance in distinguishing PDAC from each control group was assessed individually in the two sample sets. Subsequently, multiparametric modeling was applied to assess the ability of all possible two and three marker panels in distinguishing PDAC from disease-free controls. The models were generated using sample set B, and then validated in Sample Set A. RESULTS: Individually, all markers were significantly elevated in PDAC compared to healthy controls in at least one sample set ($p \leq 0.01$). SYCN, REG1B and AGR2 were also significantly elevated in PDAC compared to benign controls ($p \leq 0.01$), and AGR2 was significantly elevated in PDAC compared to other cancers ($p < 0.01$). CA19.9 was also assessed. Individually, CA19.9 showed the greatest area under the curve (AUC) in receiver operating characteristic (ROC) analysis when compared to the tested candidates; however when analyzed in combination, three panels (CA19.9 + REG1B (AUC of 0.88), CA19.9 + SYCN + REG1B (AUC of 0.87) and CA19.9 + AGR2 + REG1B (AUC of 0.87)) showed an AUC that was significantly greater ($p < 0.05$) than that of CA19.9 alone (AUC of 0.82). In a comparison of early-stage (Stage I-II) PDAC to disease free controls, the combination of SYCN + REG1B + CA19.9 showed the greatest AUC in both sample sets, (AUC of 0.87 and 0.92 in Sets A and B, respectively). CONCLUSIONS: Additional serum biomarkers, particularly

SYCN and REG1B, when combined with CA19.9, show promise as improved diagnostic indicators of pancreatic cancer, which therefore warrants further validation.

[332]

TÍTULO / TITLE: - A Novel Combinatorial Nanotechnology-Based Oral Chemopreventive Regimen Demonstrates Significant Suppression of Pancreatic Cancer Neoplastic Lesions.

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

REVISTA / JOURNAL: - Cancer Prev Res (Phila). 2013 Oct;6(10):1015-1025. Epub 2013 Sep 26.

●● Enlace al texto completo (gratis o de pago) [1158/1940-6207.CAPR-13-0172](#)

AUTORES / AUTHORS: - Grandhi BK; Thakkar A; Wang J; Prabhu S

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical Sciences, College of Pharmacy, Western University of Health Sciences, 309 E. 2nd Street, Pomona, CA 91766. sprabhu@westernu.edu.

RESUMEN / SUMMARY: - Pancreatic cancer is a deadly disease killing 37,000 Americans each year. Despite two decades of research on treatment options, the chances of survival are still less than 5% upon diagnosis. Recently, chemopreventive strategies have gained considerable attention as an alternative to treatment. We have previously shown significant in vitro chemopreventive effects with low-dose combinations of aspirin, curcumin, and sulforaphane (ACS) on pancreatic cancer cell lines. Here, we report the results of 24-week chemopreventive study with the oral administration of ACS combinations on the N-nitrosobis (2-oxopropyl) amine (BOP)-treated Syrian golden hamster model to suppress the progression of pancreatic intraepithelial neoplasms (PanIN) using unmodified (free drug) combinations of ACS, and nanoencapsulated (solid lipid nanoparticles; SLN) combinations of aspirin, curcumin, and free sulforaphane. The use of three different doses (low, medium, and high) of unmodified ACS combinations exhibited reduction in tumor incidence by 18%, 50%, and 68.7% respectively; whereas the modified nanoencapsulated ACS regimens reduced tumor incidence by 33%, 67%, and 75%, respectively, at 10 times lower dose compared with the free drug combinations. Similarly, although the unmodified free ACS showed a notable reduction in cell proliferation, the SLN encapsulated ACS regimens showed significant reduction in cell proliferation at 6.3%, 58.6%, and 72.8% as evidenced by proliferating cell nuclear antigen expression. Cell apoptotic indices were also upregulated by 1.5, 2.8, and 3.2 times, respectively, compared with BOP control. These studies provide a proof-of-concept for the use of an oral, low-dose, nanotechnology-based combinatorial regimen for the long-term chemoprevention of pancreatic cancer. Cancer Prev Res; 6(10); 1015-25. ©2013 AACR.

[333]

TÍTULO / TITLE: - Laparoscopic surgery is applicable for larger mucinous cystic neoplasms of the pancreas.

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

REVISTA / JOURNAL: - J Hepatobiliary Pancreat Sci. 2013 Sep 11. doi: 10.1002/jhbp.32.

●● Enlace al texto completo (gratis o de pago) [1002/jhbp.32](#)

AUTORES / AUTHORS: - Ohtsuka T; Takahata S; Takanami H; Ueda J; Mizumoto K; Shimizu S; 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: Mucinous cystic neoplasms (MCN) of the pancreas frequently develop in the distal pancreases of young women. Laparoscopic surgery can enhance cosmetic benefits and ease of surgery. This study assessed the feasibility of laparoscopic surgery for MCN. METHODS: The medical records of 21 patients pathologically diagnosed with benign MCN after laparoscopic resection were reviewed. Clinical data were compared in the 11 patients with tumors ≥ 45 mm (large tumor group) and the 10 patients with tumors < 45 mm (small tumor group). RESULTS: Laparoscopic resection was completed in all patients, including distal pancreatectomy with (n = 9) and without (n = 11) spleen preservation and enucleation for pancreatic head lesion (n = 1). Operation time, blood loss, postoperative morbidity, and hospital stay were similar in the two groups. Spleen-preserving pancreatectomy could be more frequently completed in the small MCN group (P = 0.02). No recurrence was observed during a median follow-up period of 12 months. CONCLUSIONS: Laparoscopic surgery can be completed in all patients with benign MCN, even those with large tumors, and patients with small MCN can get the additional benefit of spleen preservation.

[334]

TÍTULO / TITLE: - Dietary Energy Balance Modulation of Kras- and Ink4a/Arf+/-Driven Pancreatic Cancer: The Role of Insulin-like Growth Factor-I.

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

REVISTA / JOURNAL: - Cancer Prev Res (Phila). 2013 Oct;6(10):1046-1055. Epub 2013 Aug 26.

●● Enlace al texto completo (gratis o de pago) [1158/1940-6207.CAPR-13-](#)

[0185](#)

AUTORES / AUTHORS: - Lashinger LM; Harrison LM; Rasmussen AJ; Logsdon CD; Fischer SM; McArthur MJ; Hursting SD

INSTITUCIÓN / INSTITUTION: - Department of Nutritional Sciences, Dell Pediatric Research Institute, University of Texas at Austin, 1400 Barbara Jordan Blvd. Mail Code R1800, Austin, TX 78723. shursting@austin.utexas.edu.

RESUMEN / SUMMARY: - New molecular targets and intervention strategies for breaking the obesity-pancreatic cancer link are urgently needed. Using relevant spontaneous

and orthotopically transplanted murine models of pancreatic cancer, we tested the hypothesis that dietary energy balance modulation impacts pancreatic cancer development and progression through an insulin-like growth factor (IGF)-I-dependent mechanism. In LSL-KrasG12D/Pdx-1-Cre/Ink4a/Arflox/+ mice, calorie restriction versus overweight- or obesity-inducing diet regimens decreased serum IGF-I, tumoral Akt/mTOR signaling, pancreatic desmoplasia, and progression to pancreatic ductal adenocarcinoma (PDAC), and increased pancreatic tumor-free survival. Serum IGF-I, Akt/mTOR signaling, and orthotopically transplanted PDAC growth were decreased in liver-specific IGF-I-deficient mice (vs. wild-type mice), and rescued with IGF-I infusion. Thus, dietary energy balance modulation impacts spontaneous pancreatic tumorigenesis induced by mutant Kras and Ink4a deficiency, the most common genetic alterations in human pancreatic cancer. Furthermore, IGF-I and components of its downstream signaling pathway are promising mechanistic targets for breaking the obesity-pancreatic cancer link. *Cancer Prev Res*; 6(10); 1046-55. ©2013 AACR.

[335]

TÍTULO / TITLE: - Structural and logical analysis of a comprehensive hedgehog signaling pathway to identify alternative drug targets for glioma, colon and pancreatic cancer.

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

REVISTA / JOURNAL: - *PLoS One*. 2013 Jul 23;8(7):e69132. doi: 10.1371/journal.pone.0069132. Print 2013.

●● Enlace al texto completo (gratis o de pago) 1371/journal.pone.0069132

AUTORES / AUTHORS: - Chowdhury S; Pradhan RN; Sarkar RR

INSTITUCIÓN / INSTITUTION: - Chemical Engineering and Process Development, CSIR-National Chemical Laboratory, Pune, Maharashtra, India.

RESUMEN / SUMMARY: - Hedgehog is an evolutionarily conserved developmental pathway, widely implicated in controlling various cellular responses such as cellular proliferation and stem cell renewal in human and other organisms, through external stimuli. Aberrant activation of this pathway in human adult stem cell line may cause different types of cancers. Hence, targeting this pathway in cancer therapy has become indispensable, but the non availability of detailed molecular interactions, complex regulations by extra- and intra-cellular proteins and cross talks with other pathways pose a serious challenge to get a coherent understanding of this signaling pathway for making therapeutic strategy. This motivated us to perform a computational study of the pathway and to identify probable drug targets. In this work, from available databases and literature, we reconstructed a complete hedgehog pathway which reports the largest number of molecules and interactions to date. Using recently developed computational techniques, we further performed structural and logical analysis of this pathway. In structural analysis, the connectivity and centrality parameters were calculated to identify the important proteins from the network. To capture the regulations of the molecules, we developed a master Boolean

model of all the interactions between the proteins and created different cancer scenarios, such as Glioma, Colon and Pancreatic. We performed perturbation analysis on these cancer conditions to identify the important and minimal combinations of proteins that can be used as drug targets. From our study we observed the under expressions of various oncoproteins in Hedgehog pathway while perturbing at a time the combinations of the proteins GLI1, GLI2 and SMO in Glioma; SMO, HFU, ULK3 and RAS in Colon cancer; SMO, HFU, ULK3, RAS and ERK12 in Pancreatic cancer. This reconstructed Hedgehog signaling pathway and the computational analysis for identifying new combinatory drug targets will be useful for future in-vitro and in-vivo analysis to control different cancers.

[336]

TÍTULO / TITLE: - Mammalian target of rapamycin signaling activation patterns in pancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - J Hepatobiliary Pancreat Sci. 2013 Sep 3. doi: 10.1002/jhbp.26.

●● [Enlace al texto completo \(gratis o de pago\) 1002/jhbp.26](#)

AUTORES / AUTHORS: - Komori Y; Yada K; Ohta M; Uchida H; Iwashita Y; Fukuzawa K; Kashima K; Yokoyama S; Inomata M; Kitano S

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological and Pediatric Surgery, Oita University Faculty of Medicine, 1-1 Idaigaoka, Hasama-machi, Yufu, Oita, 879-5593, Japan. komorin@oita-u.ac.jp.

RESUMEN / SUMMARY: - BACKGROUND: Phosphatidylinositol 3-kinase/Akt/mammalian target of rapamycin (mTOR) pathway dysregulation has been implicated in the development of various human cancers. However, expression of mTOR cascade components in pancreatic neuroendocrine tumors (PNETs) has not been fully explored. The aim of this study was to assess the expression of mTOR pathway in PNETs using immunohistochemistry. METHODS: From December 1984 to April 2012, we surgically treated 42 patients with PNETs. We used immunohistochemistry to evaluate expression of mTOR, phosphorylated mTOR (p-mTOR), p70S6 kinase (S6K), phosphorylated S6 ribosomal protein (p-S6rp), eukaryotic initiation factor 4E-binding protein 1 (4E-BP1), and phosphorylated 4E-BP1 (p-4E-BP1) in the resected specimens. The relation between the expression of these molecules and clinicopathological characteristics was investigated. RESULTS: We identified the expression of mTOR (28.6%), p-mTOR (52.4%), S6K (52.4%), p-S6rp (40.5%), 4E-BP1 (81.0%), and p-4E-BP1 (26.2%) in PNETs. The expression of mTOR, p-mTOR, S6K, and p-S6rp was significantly associated with tumor invasion, proliferation, and an advanced-stage. Particularly, the expression of p-mTOR was related to clinically relevant factors such as tumor size, vascular invasion, extrapancreatic invasion, lymph node and/or distant metastasis, mitotic count, and European Neuroendocrine Tumor Society TNM staging as well as the 2004 and 2010 World Health Organization (WHO) classification. In addition, p-S6rp

expression was related to vascular invasion, extrapancreatic invasion, lymph node and distant metastasis, mitotic count, and the 2010 WHO classification. In contrast, no significant relation between 4E-BP1 activation and clinicopathological factors was observed. The expression of p-mTOR was strongly correlated with that of p-S6rp ($r = 0.474$, $P = 0.002$). CONCLUSIONS: Our results suggest that activation of the mTOR/S6K signaling pathway plays a significant role in tumorigenesis and progression of PNET.

[337]

TÍTULO / TITLE: - Notch Signaling Pathway in Pancreatic Cancer Progression.

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

REVISTA / JOURNAL: - Pancreat Disord Ther. 2013 May 30;3(114). pii: 1000114.

AUTORES / AUTHORS: - Ma J; Xia J; Miele L; Sarkar FH; Wang Z

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Bengbu Medical College, Anhui, PR China.

[338]

TÍTULO / TITLE: - DCLK1 Regulates Pluripotency and Angiogenic Factors via microRNA-Dependent Mechanisms in Pancreatic Cancer.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 9;8(9):e73940. doi: 10.1371/journal.pone.0073940.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0073940](#)

AUTORES / AUTHORS: - Sureban SM; May R; Qu D; Weygant N; Chandrakesan P; Ali N; Lightfoot SA; Pantazis P; Rao CV; Postier RG; Houchen CW

INSTITUCIÓN / INSTITUTION: - Department of Medicine, the University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, United States of America ; Department of Veterans Affairs Medical Center, Oklahoma City, Oklahoma, United States of America ; The Peggy and Charles Stephenson Cancer Center, Oklahoma City, Oklahoma, United States of America.

RESUMEN / SUMMARY: - Stem cell pluripotency, angiogenesis and epithelial-mesenchymal transition (EMT) have been shown to be significantly upregulated in pancreatic ductal adenocarcinoma (PDAC) and many other aggressive cancers. The dysregulation of these processes is believed to play key roles in tumor initiation, progression, and metastasis, and is contributory to PDAC being the fourth leading cause of cancer-related deaths in the US. The tumor suppressor miRNA miR-145 downregulates critical pluripotency factors and oncogenes and results in repressed metastatic potential in PDAC. Additionally, the miR-200 family regulates several angiogenic factors which have been linked to metastasis in many solid tumors. We have previously demonstrated that downregulation of DCLK1 can upregulate critical miRNAs in both in vitro and in vivo cancer models and results in downregulation of c-MYC, KRAS, NOTCH1 and EMT-related transcription factors. A recent report has also

shown that Dclk1 can distinguish between normal and tumor stem cells in Apc (min/+) mice and that ablation of Dclk1(+) cells resulted in regression of intestinal polyps without affecting homeostasis. Here we demonstrate that the knockdown of DCLK1 using poly(lactide-co-glycolide)-encapsulated-DCLK1-siRNA results in AsPC1 tumor growth arrest. Examination of xenograft tumors revealed, (a) increased miR-145 which results in decreased pluripotency maintenance factors OCT4, SOX2, NANOG, KLF4 as well as KRAS and RREB1; (b) increased let-7^a which results in decreased pluripotency factor LIN28B; and (c) increased miR-200 which results in decreased VEGFR1, VEGFR2 and EMT-related transcription factors ZEB1, ZEB2, SNAIL and SLUG. Specificity of DCLK1 post-transcriptional regulation of the downstream targets of miR-145, miR-200 and let-7^a was accomplished utilizing a luciferase-based reporter assay. We conclude that DCLK1 plays a significant master regulatory role in pancreatic tumorigenesis through the regulation of multiple tumor suppressor miRNAs and their downstream pro-tumorigenic pathways. This novel concept of targeting DCLK1 alone has several advantages over targeting single pathway or miRNA-based therapies for PDAC.

[339]

TÍTULO / TITLE: - Pancreatic neuroendocrine tumours: hypoenhancement on arterial phase computed tomography predicts biological aggressiveness.

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

REVISTA / JOURNAL: - HPB (Oxford). 2013 Aug 29. doi: 10.1111/hpb.12139.

●● [Enlace al texto completo \(gratis o de pago\) 1111/hpb.12139](#)

AUTORES / AUTHORS: - Worhunsky DJ; Krampitz GW; Poullos PD; Visser BC; Kunz PL; Fisher GA; Norton JA; Poultides GA

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Division of Oncology, Stanford University Medical Center, Stanford, CA, USA.

RESUMEN / SUMMARY: - BACKGROUND: Contrary to pancreatic adenocarcinoma, pancreatic neuroendocrine tumours (PNET) are commonly hyperenhancing on arterial phase computed tomography (APCT). However, a subset of these tumours can be hypoenhancing. The prognostic significance of the CT appearance of these tumors remains unclear. METHODS: From 2001 to 2012, 146 patients with well-differentiated PNET underwent surgical resection. The degree of tumour enhancement on APCT was recorded and correlated with clinicopathological variables and overall survival.

RESULTS: APCT images were available for re-review in 118 patients (81%). The majority had hyperenhancing tumours (n = 80, 68%), 12 (10%) were isoenhancing (including cases where no mass was visualized) and 26 (22%) were hypoenhancing.

Hypoenhancing PNET were larger, more commonly intermediate grade, and had higher rates of lymph node and synchronous liver metastases. Hypoenhancing PNET were also associated with significantly worse overall survival after a resection as opposed to isoenhancing and hyperenhancing tumours (5-year, 54% versus 89% versus 93%). On multivariate analysis of factors available pre-operatively, only hypoenhancement (HR

2.32, P = 0.02) was independently associated with survival. DISCUSSION: Hypoenhancement on APCT was noted in 22% of well-differentiated PNET and was an independent predictor of poor outcome. This information can inform pre-operative decisions in the multidisciplinary treatment of these neoplasms.

[340]

TÍTULO / TITLE: - Metastatic pancreatic carcinoma and bronchioloalveolar adenomas in an Egyptian fruit bat (*Rousettus aegyptiacus*).

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

REVISTA / JOURNAL: - J Zoo Wildl Med. 2013 Sep;44(3):794-8.

AUTORES / AUTHORS: - Cushing AC; Ossiboff R; Buckles E; Abou-Madi N

INSTITUCIÓN / INSTITUTION: - Section of Zoological Medicine, Department of Clinical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, New York 14853, USA. acc323@cornell.edu

RESUMEN / SUMMARY: - An adult female, intact Egyptian fruit bat (*Rousettus aegyptiacus*) was presented for lethargy, anorexia, and markedly reduced flying activity. Physical and ultrasound examinations were suggestive of an abdominal mass with free fluid within the abdomen. Based on the poor and deteriorating clinical condition of the animal, euthanasia was elected. Gross necropsy revealed an irregular thickening at the root of the mesentery and a diffusely, dark-red liver with rounded hepatic margins. Histologic examination revealed extensive neoplastic effacement of the pancreas with invasion into the surrounding mesentery and mesenteric lymph nodes and metastatic spread to the liver. Based on the morphology of the neoplastic cells, the involvement of the pancreas, and immunohistochemistry, a diagnosis of metastatic pancreatic carcinoma was made. Additionally, two small neoplasms were identified in the lungs. These masses were distinct from the carcinoma, and their morphology was consistent with bronchioloalveolar adenomas. This is the first known report of either benign pulmonary lesions or pancreatic carcinomas in the order Chiroptera.

[341]

TÍTULO / TITLE: - PGP 9.5 immunocytochemical staining for pancreatic endocrine tumors.

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

REVISTA / JOURNAL: - Islets. 2013 Jun 27;5(3).

AUTORES / AUTHORS: - Tomita T

INSTITUCIÓN / INSTITUTION: - Departments of Integrative Biosciences and Pathology; Oregon National Primate Center; Oregon Health and Science University; Portland, OR USA.

RESUMEN / SUMMARY: - Aims/hypothesis: Protein gene product 9.5 (PGP 9.5) is a marker for neuroendocrine cells but has not been used for pancreatic islet cells and pancreatic endocrine tumors (PETs). Antibodies for PGP 9.5 are now commercially available for immunocytochemical study, with which immunostaining may be able to differentiate between benign and malignant PETs. Results: All 4 kinds of normal islet cells were positively immunostained for PGP 9.5-moderately positive for beta-cells and strongly positive for delta-cells, whereas ganglion cells were immunostained more strongly than islet cells. Nine of 12 insulinomas were moderately to strongly positive for PGP 9.5. Two glucagonomas, 3 of 6 pancreatic polypeptidomas (PPomas), 3 of 9 gastrinomas, and 2 of 4 non-functioning PETs were negative for PGP 9.5. Conclusion/Interpretation: PGP 9.5 immunostaining was universally positive for 4 kinds of islet cells and was moderately to strongly positive for 9 of 12 (75%) insulinomas. All 22 non-beta-cell PETs were negative or weakly positive for PGP 9.5, and thus negative or weakly positive PGP 9.5 immunostaining may be used as a marker for potential malignancy and poor prognosis for non-beta-cell PETs. Materials and Methods: Thirty-four PETs were immunocytochemically stained for PGP 9.5 using a rabbit polyclonal antibody together with immunostaining for 4 pancreatic hormones, chromogranin A (CgA), and gastrin. PETs consisted of 12 insulinomas, 2 glucagonomas, 1 somatostatinoma (SRIFoma), 6 PPomas, 9 gastrinomas, and 4 non-functioning PETs.

[342]

TÍTULO / TITLE: - Rapid dramatic alterations to the tumor microstructure in pancreatic cancer following irreversible electroporation ablation.

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

REVISTA / JOURNAL: - Nanomedicine (Lond). 2013 Sep 11.

●● [Enlace al texto completo \(gratis o de pago\) 2217/nnm.13.72](#)

AUTORES / AUTHORS: - Zhang Z; Li W; Procissi D; Tyler P; Omary RA; Larson AC

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Northwestern University, 737 N. Michigan Avenue, 16th Floor, Chicago, IL 60611, USA.

RESUMEN / SUMMARY: - Aim: NanoKnife® (Angiodynamics, Inc., NY, USA) or irreversible electroporation (IRE) is a newly available ablation technique to induce the formation of nanoscale pores within the cell membrane in targeted tissues. The purpose of this study was to elucidate morphological alterations following 30 min of IRE ablation in a mouse model of pancreatic cancer. Materials & methods: Immunohistochemistry markers were compared with diffusion-weighted MRI apparent diffusion coefficient measurements before and after IRE ablation. Results: Immunohistochemistry apoptosis index measurements were significantly higher in IRE-treated tumors than in controls. Rapid tissue alterations after 30 min of IRE ablation procedures (structural and morphological alterations along with significantly elevated apoptosis markers) were consistently observed and well correlated to apparent diffusion coefficient measurements. Discussion: This imaging assay offers the potential to serve as an in

vivo biomarker for noninvasive detection of tumor response following IRE ablation.
Original submitted 2 October 2012; Revised submitted 12 March 2013.

[343]

TÍTULO / TITLE: - Effects of tobacco constituents and psychological stress on the beta-adrenergic regulation of non-small cell lung cancer and pancreatic cancer: implications for intervention.

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

REVISTA / JOURNAL: - Cancer Biomark. 2013;13(3):133-44. doi: 10.3233/CBM-130323.

●● Enlace al texto completo (gratis o de pago) [3233/CBM-130323](#)

AUTORES / AUTHORS: - Schuller HM

INSTITUCIÓN / INSTITUTION: - Experimental Oncology Laboratory, Department of Biomedical and Diagnostic Sciences, College of Veterinary Medicine, University of Tennessee, 2407 River Drive Knoxville, TN 37996, USA. hmsch@utk.edu

RESUMEN / SUMMARY: - This review summarizes current preclinical and clinical evidence in support of the hypothesis that smoking and psychological stress have significant cancer promoting effects on non small cell lung cancer and pancreatic cancer via direct and indirect effects on nicotinic receptor-regulated beta-adrenergic signaling. Evidence is provided that targeted pharmacological interference with the resulting hyperactive cAMP-dependent signaling by beta-blockers or by gamma-aminobutyric acid as well as positive psychological influences may be highly effective in preventing and improving clinical outcomes of these cancers, provided that appropriate diagnostic protocols are followed to monitor systemic levels of stress neurotransmitters and cAMP.

[344]

TÍTULO / TITLE: - Ron knockdown and Ron monoclonal antibody IMC-RON8 sensitize pancreatic cancer to histone deacetylase inhibitors (HDACi).

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

REVISTA / JOURNAL: - PLoS One. 2013 Jul 29;8(7):e69992. doi: 10.1371/journal.pone.0069992. Print 2013.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0069992](#)

AUTORES / AUTHORS: - Zou Y; Howell GM; Humphrey LE; Wang J; Brattain MG

INSTITUCIÓN / INSTITUTION: - Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, Nebraska, United States of America.

RESUMEN / SUMMARY: - Recepteur d'origine nantais (Ron) is overexpressed in a panel of pancreatic cancer cells and tissue samples from pancreatic cancer patients. Ron can be activated by its ligand macrophage stimulating protein (MSP), thereby activating oncogenic signaling pathways. Crosstalk between Ron and EGFR, c-Met, or IGF-1R may provide a mechanism underlying drug resistance. Thus, targeting Ron may represent a novel therapeutic strategy. IMC-RON8 is the first Ron monoclonal antibody (mAb) entering clinical trial for targeting Ron overexpression. Our studies show IMC-RON8

downmodulated Ron expression in pancreatic cancer cells and significantly blocked MSP-stimulated Ron activation, downstream Akt and ERK phosphorylation, and survivin mRNA expression. IMC-RON8 hindered MSP-induced cell migration and reduced cell transformation. Histone deacetylase inhibitors (HDACi) are reported to target expression of various genes through modification of nucleosome histones and non-histone proteins. Our work shows HDACi TSA and Panobinostat (PS) decreased Ron mRNA and protein expression in pancreatic cancer cells. PS also reduced downstream signaling of pAkt, survivin, and XIAP, as well as enhanced cell apoptosis. Interestingly, PS reduced colony formation in Ron knockdown cells to a greater extent than Ron scramble control cells in colony formation and soft agarose assays. IMC-RON8 could also sensitize pancreatic cancer cells to PS, as reflected by reduced colony numbers and size in combination treatment with IMC-RON8 and PS compared to single treatment alone. The co-treatment further reduced Ron expression and pAkt, and increased PARP cleavage compared to either treatment alone. This study suggests the potential for a novel combination approach which may ultimately be of value in treatment of pancreatic cancer.

[345]

TÍTULO / TITLE: - Hepatic Artery Embolization prior to En Bloc Resection of an Encased Common Hepatic Artery in Adenocarcinoma of the Head of the Pancreas.

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

REVISTA / JOURNAL: - Case Rep Med. 2013;2013:205475. doi: 10.1155/2013/205475. Epub 2013 Aug 4.

●● Enlace al texto completo (gratis o de pago) [1155/2013/205475](#)

AUTORES / AUTHORS: - Sergeant G; Schadde E; Maleux G; Aerts R

INSTITUCIÓN / INSTITUTION: - Department of Abdominal Surgery, University Hospital Leuven, Herestraat 49, 3000 Leuven, Belgium ; Swiss HPB Center, Department for Visceral and Transplantation Surgery, University Hospital Zurich, 8091 Zurich, Switzerland.

RESUMEN / SUMMARY: - A 64-year-old female patient with adenocarcinoma of the head of the pancreas with encasement of the common hepatic artery and portal vein stenosis was reexplored after six cycles of gemcitabine (1000 mg/m²). Prior to surgery, the patient underwent balloon dilation and stenting of the portal vein in addition to successful coil embolisation of the common hepatic artery, proper hepatic artery, and proximal gastroduodenal artery. After embolisation, a pylorus-preserving pancreaticoduodenectomy was performed with resection of the common hepatic artery and portal vein confluents. Pathological examination showed a moderately differentiated pT3N0 (Stage IIa, TNM 7th edition) tumor with negative section margins. We show with this case that in selected cases of periampullary cancer with encasement of the common hepatic artery, it is technically feasible to perform pancreaticoduodenectomy with hepatic artery resection and negative surgical margins.

Nevertheless, the oncological benefit of extended arterial resections remains controversial.

[346]

TÍTULO / TITLE: - Cytological criteria of high-grade epithelial atypia in the cyst fluid of pancreatic intraductal papillary mucinous neoplasms.

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

REVISTA / JOURNAL: - Cancer Cytopathol. 2013 Aug 12. doi: 10.1002/cncy.21344.

●● Enlace al texto completo (gratis o de pago) [1002/cncy.21344](#)

AUTORES / AUTHORS: - Pitman MB; Centeno BA; Dagiilar ES; Brugge WR; Mino-Kenudson M

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts.

RESUMEN / SUMMARY: - BACKGROUND: The recognition of epithelial cells with high-grade atypia (HGA) in the cyst fluid of an intraductal papillary mucinous neoplasm (IPMN) identifies a cyst at high risk of invasive carcinoma. To the best of the authors' knowledge, the cytological features of HGA have not been systematically analyzed to define diagnostic criteria. METHODS: Cell groups from patients with histologically confirmed branch-duct IPMNs were evaluated by 2 cytopathologists with expertise in pancreatic cytology. A consensus interpretation categorized the cell groups as having either low-grade (LG) or high-grade (HG) morphology. Characteristics regarding cell size and architecture, nuclear and cytoplasmic features, and background necrosis were analyzed. Performance characteristics were assessed using the Fisher exact test at 95% confidence intervals. RESULTS: Sixty cell groups yielded 27 LG and 25 HG morphological groups. No consensus was reached for 8 groups, which were excluded from statistical analysis. Five features that were found to be significantly different between the LG and HG groups included: 1) cell size < a 12-mum duodenal enterocyte for HG and size equal for LG; 2) an increased nuclear-to-cytoplasmic (N/C) ratio; 3) marked nuclear membrane abnormalities; 4) abnormal chromatin pattern; and 5) background necrosis. The 3 most accurate features for the identification of HGA were background necrosis (88%), abnormal chromatin pattern (84%), and an increased N/C ratio (82%). CONCLUSIONS: IPMN cyst fluid at high-risk of malignancy can be recognized most accurately by the presence of epithelial cells with HGA showing an increased N/C ratio, an abnormal chromatin pattern, and background necrosis. Cancer (Cancer Cytopathol) 2013. © 2013 American Cancer Society.

[347]

TÍTULO / TITLE: - Single incision laparoscopic distal pancreatectomy with splenectomy for neuroendocrine tumor of the tail of pancreas.

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

REVISTA / JOURNAL: - J Minim Access Surg. 2013 Jul;9(3):132-5. doi: 10.4103/0972-9941.115377.

●● Enlace al texto completo (gratis o de pago) [4103/0972-9941.115377](https://doi.org/10.4103/0972-9941.115377)

AUTORES / AUTHORS: - Srikanth G; Shetty N; Dubey D

INSTITUCIÓN / INSTITUTION: - Department of Surgical Gastroenterology, MILDD, Manipal Hospital, Bangalore, India.

RESUMEN / SUMMARY: - Laparoscopic resection is becoming the standard of care for tumors located in the body and tail of pancreas. We herein report a patient with neuroendocrine tumor in the tail of pancreas who underwent single incision laparoscopic distal pancreatectomy with splenectomy without the use of a commercial port device.

[348]

TÍTULO / TITLE: - The Anti-Tumor Effect of HDAC Inhibition in a Human Pancreas Cancer Model Is Significantly Improved by the Simultaneous Inhibition of Cyclooxygenase 2.

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

REVISTA / JOURNAL: - PLoS One. 2013 Sep 11;8(9):e75102. doi: 10.1371/journal.pone.0075102.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0075102](https://doi.org/10.1371/journal.pone.0075102)

AUTORES / AUTHORS: - Peulen O; Gonzalez A; Peixoto P; Turtoi A; Mottet D; Delvenne P; Castronovo V

INSTITUCIÓN / INSTITUTION: - Metastasis Research Laboratory, GIGA-Cancer, University of Liege, Liege, Belgium.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma is the fourth leading cause of cancer death worldwide, with no satisfactory treatment to date. In this study, we tested whether the combined inhibition of cyclooxygenase-2 (COX-2) and class I histone deacetylase (HDAC) may result in a better control of pancreatic ductal adenocarcinoma. The impact of the concomitant HDAC and COX-2 inhibition on cell growth, apoptosis and cell cycle was assessed first in vitro on human pancreas BxPC-3, PANC-1 or CFPAC-1 cells treated with chemical inhibitors (SAHA, MS-275 and celecoxib) or HDAC1/2/3/7 siRNA. To test the potential antitumoral activity of this combination in vivo, we have developed and characterized, a refined chick chorioallantoic membrane tumor model that histologically and proteomically mimics human pancreatic ductal adenocarcinoma. The combination of HDAC1/3 and COX-2 inhibition significantly impaired proliferation of BxPC-3 cells in vitro and stalled entirely the BxPC-3 cells tumor growth onto the chorioallantoic membrane in vivo. The combination was more effective than either drug used alone. Consistently, we showed that both HDAC1 and HDAC3 inhibition induced the expression of COX-2 via the NF-κB pathway. Our data demonstrate, for the first time in a Pancreatic Ductal Adenocarcinoma (PDAC) model, a significant action of HDAC and COX-2 inhibitors on

cancer cell growth, which sets the basis for the development of potentially effective new combinatory therapies for pancreatic ductal adenocarcinoma patients.

[349]

TÍTULO / TITLE: - A bioengineered heterotypic stroma-cancer microenvironment model to study pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Lab Chip. 2013 Aug 27;13(19):3965-75. doi: 10.1039/c3lc50487e.

●● Enlace al texto completo (gratis o de pago) [1039/c3lc50487e](#)

AUTORES / AUTHORS: - Drifka CR; Eliceiri KW; Weber SM; Kao WJ

INSTITUCIÓN / INSTITUTION: - Department of Biomedical Engineering, University of Wisconsin, Madison, WI, USA.

RESUMEN / SUMMARY: - Interactions between neoplastic epithelial cells and components of a reactive stroma in pancreatic ductal adenocarcinoma (PDAC) are of key significance behind the disease's dismal prognosis. Despite extensive published research in the importance of stroma-cancer interactions in other cancers and experimental evidence supporting the importance of the microenvironment in PDAC progression, a reproducible three-dimensional (3D) in vitro model for exploring stroma-cancer interplay and evaluating therapeutics in a physiologically relevant context has been lacking. We introduce a humanized microfluidic model of the PDAC microenvironment incorporating multicellularity, extracellular matrix (ECM) components, and a spatially defined 3D microarchitecture. Pancreatic stellate cells (PSCs) isolated from clinically-evaluated human tissue specimens were co-cultured with pancreatic ductal adenocarcinoma cells as an accessible 3D construct that maintained important tissue features and disease behavior. Multiphoton excitation (MPE) and Second Harmonic Generation (SHG) imaging techniques were utilized to image the intrinsic signal of stromal collagen in human pancreatic tissues and live cell-collagen interactions within the optically-accessible microfluidic tissue model. We further evaluated the dose-response of the model with the anticancer agent paclitaxel. This bioengineered model of the PDAC stroma-cancer microenvironment provides a complementary platform to elucidate the complex stroma-cancer interrelationship and to evaluate the efficacy of potential therapeutics in a humanized system that closely recapitulates key PDAC microenvironment characteristics.

[350]

TÍTULO / TITLE: - Obstructive Jaundice due to Pancreatic Metastasis from Non-small Cell Lung Cancer.

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

REVISTA / JOURNAL: - Acta Med Indones. 2013 Jul;45(3):216-9.

AUTORES / AUTHORS: - Bestari MB; Agustanti N

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Faculty of Medicine, Padjadjaran University - Hasan Sadikin Hospital, Bandung, Indonesia.

RESUMEN / SUMMARY: - We report a 67-year-old female patient, recently diagnosed to have non-small cell lung cancer (NSCLC). On first PET (positron emission tomography) examination in October 2009, no distant metastasis. Four months later, second PET examination was done, detecting pancreatic foci in the uncinata process and in the tail of the pancreas measuring 22 mm which were more likely to be metastatic rather than primary origin. The patient underwent chemotherapy and radiotherapy. After 1 month of follow up, jaundice was noticed. Laboratory exams and MRCP showed obstructive jaundice. ERCP was performed with biliary stenting for palliative treatment. Symptomatic metastatic lesions of the pancreas from carcinoma of the lung are extremely rare. Typically, the patients remain asymptomatic until their disease reaches a fairly advanced stage, and therapeutic options are then limited to palliative measures.

PTPTPTP - Journal Article

[351]

TÍTULO / TITLE: - Pancreatic pseudocyst or a cystic tumor of the pancreas?

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

REVISTA / JOURNAL: - Chin J Cancer. 2013 Aug 6. doi: 10.5732/cjc.012.10296.

●● [Enlace al texto completo \(gratis o de pago\) 5732/cjc.012.10296](#)

AUTORES / AUTHORS: - Rabie ME; Hakeem IE; Skaini MS; Hadad AE; Jamil S; Shah MT; Obaid M

INSTITUCIÓN / INSTITUTION: - 1Department of Surgery, Armed Forces Hospital-Southern Region, PO Box 101, Khamis Mushait, Saudi Arabia. ezzedien@hotmail.com.

RESUMEN / SUMMARY: - Pancreatic pseudocysts are the most common cystic lesions of the pancreas and may complicate acute pancreatitis, chronic pancreatitis, or pancreatic trauma. While the majority of acute pseudocysts resolve spontaneously, few may require drainage. On the other hand, pancreatic cystic tumors, which usually require extirpation, may disguise as pseudocysts. Hence, the distinction between the two entities is crucial for a successful outcome. We conducted this study to highlight the fundamental differences between pancreatic pseudocysts and cystic tumors so that relevant management plans can be devised. We reviewed the data of patients with pancreatic cystic lesions that needed intervention between June 2007 and December 2010 in our hospital. We identified 9 patients (5 males and 4 females) with a median age of 40 years (range, 30--70 years). Five patients had pseudocysts, 2 had cystic tumors, and 2 had undetermined pathology. Pancreatic pseudocysts were treated by pseudocystogastrostomy in 2 cases and percutaneous drainage in 3 cases. In one case, recurrence occurred after percutaneous drainage and required pseudocystogastrostomy. The true pancreatic cysts were serous cystadenoma, which was treated by distal pancreatectomy, and mucinous cystadenocarcinoma, which was

initially treated by drainage, like a pseudocyst, and then by distal pancreatectomy when its true nature was revealed. We conclude that every effort should be exerted to distinguish between pancreatic pseudocysts and cystic tumors of the pancreas to avoid the serious misjudgment of draining rather than extirpating a pancreatic cystic tumor. Additionally, percutaneous drainage of a pancreatic pseudocyst is a useful adjunct that may substitute for surgical drainage.

[352]

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

REVISTA / JOURNAL: - Cancer Cytopathol. 2013 Sep;121(9):471-2. doi: 10.1002/cncy.21341.

●● Enlace al texto completo (gratis o de pago) [1002/cncy.21341](#)

AUTORES / AUTHORS: - Forcione DG

INSTITUCIÓN / INSTITUTION: - Gastrointestinal Unit, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts.

[353]

TÍTULO / TITLE: - Mimics of pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Cancer Imaging. 2013 Sep 23;13(3):342-9. doi: 10.1102/1470-7330.2013.9012.

●● Enlace al texto completo (gratis o de pago) [1102/1470-7330.2013.9012](#)

AUTORES / AUTHORS: - Al-Hawary MM; Kaza RK; Azar SF; Ruma JA; Francis IR

INSTITUCIÓN / INSTITUTION: - Department of Radiology, University of Michigan Health Services, Ann Arbor, MI, USA.

RESUMEN / SUMMARY: - Several uncommon primary pancreatic tumors, inflammatory conditions, metastasis to the pancreas and peripancreatic masses can mimic the appearance of pancreatic ductal adenocarcinoma (PDA). Differentiation between these lesions and PDA can be challenging, due to the overlap in imaging features; however, familiarity with their typical imaging features and clinical presentation may be helpful in their differentiation, as in some cases, invasive diagnostic tests or unnecessary surgery can be avoided. The different pathologies that can mimic PDA include inflammatory conditions such as the various forms of pancreatitis (chronic-focal mass-forming, autoimmune and groove pancreatitis), pancreatic neuroendocrine tumors, solid pseudopapillary tumors, metastasis (solid non-lymphomatous and hematologic), congenital variants (annular pancreas), as well as peripancreatic lesions (accessory spleen, adrenal masses, duodenal masses, lymph nodes and vascular lesions), and certain rare pancreatic tumors (e.g., acinar cell tumors, solid serous tumors, hamartoma and solitary fibrous tumors). The clinical presentation and imaging features of the most commonly encountered mimics of PDA are discussed in this presentation with representative illustrations.

[354]

TÍTULO / TITLE: - Increased B cell-activating factor promotes tumor invasion and metastasis in human pancreatic cancer.

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

REVISTA / JOURNAL: - PLoS One. 2013 Aug 6;8(8):e71367. doi: 10.1371/journal.pone.0071367. Print 2013.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0071367](#)

AUTORES / AUTHORS: - Koizumi M; Hiasa Y; Kumagi T; Yamanishi H; Azemoto N; Kobata T; Matsuura B; Abe M; Onji M

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology and Metabolism, Ehime University Graduate School of Medicine, Ehime, Japan.

RESUMEN / SUMMARY: - B cell-activating factor (BAFF) is a cytokine belonging to the tumor necrosis factor (TNF) superfamily. It has been reported that BAFF is elevated in patients with autoimmune pancreatitis and contributes to the malignant potential of blood cancers and solid tumors. In this study, clinical evidence of increased BAFF levels in patients with pancreatic ductal adenocarcinoma (PDAC) was obtained, and the roles and mechanisms of BAFF in PDAC were clarified in human tissues of PDAC and from in vitro data of PDAC cell lines. Serum levels of BAFF in patients with PDAC were significantly higher than in healthy subjects ($p = 0.0121$). Patients with UICC stage IV PDAC (T1-4, N0-1, M1) had significantly higher levels of serum BAFF compared to patients with PDAC ($p = 0.0182$). BAFF was remarkably expressed in infiltrating B lymphocytes surrounding pancreatic cancer in human pancreatic tissues, suggesting that BAFF may play a role in progression of pancreatic cancer. PDAC cell lines were cultured with human recombinant BAFF, and morphology and gene expression were analyzed; pancreatic cancer cells changed to a fibroblast-like morphology, and showed altered gene expression of E-cadherin, vimentin and Snail. These BAFF-induced changes reflect enhanced cell motility and invasion. BAFF-R-overexpressing cell clones confirmed the association between these BAFF-induced changes and epithelial-mesenchymal transition (EMT)-related genes. BAFF was elevated in patients with metastatic advanced PDAC and induced alterations in PDAC cells via regulation of EMT-related genes. Elucidation of the precise role and mechanism of control of BAFF may lead to new therapeutic approaches with the aim of improving pancreatic cancer survival.

[355]

TÍTULO / TITLE: - Integrative genomic and functional profiling of the pancreatic cancer genome.

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

REVISTA / JOURNAL: - BMC Genomics. 2013 Sep 16;14(1):624.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2164-14-624](#)

AUTORES / AUTHORS: - Shain AH; Salari K; Giacomini CP; Pollack JR

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is a deadly disease with a five-year survival of less than 5%. A better understanding of the underlying biology may suggest novel therapeutic targets. Recent surveys of the pancreatic cancer genome have uncovered numerous new alterations; yet systematic functional characterization of candidate cancer genes has lagged behind. To address this challenge, here we have devised a highly-parallel RNA interference-based functional screen to evaluate many genomically-nominated candidate pancreatic cancer genes simultaneously. RESULTS: For 185 candidate pancreatic cancer genes, selected from recurrently altered genomic loci, we performed a pooled shRNA library screen of cell growth/viability across 10 different cell lines. Knockdown-associated effects on cell growth were assessed by enrichment or depletion of shRNA hairpins, by hybridization to barcode microarrays. A novel analytical approach (CORrelated Phenotypes for On-Target Effects; COPOTE) was used to discern probable on-target knockdown, based on identifying different shRNAs targeting the same gene and displaying concordant phenotypes across cell lines. Knockdown data were integrated with genomic architecture and gene-expression profiles, and selected findings validated using individual shRNAs and/or independent siRNAs. The pooled shRNA library design delivered reproducible data. In all, COPOTE analysis identified 52 probable on-target gene-knockdowns. Knockdown of known oncogenes (KRAS, MYC, SMURF1 and CCNE1) and a tumor suppressor (CDKN2A) showed the expected contrasting effects on cell growth. In addition, the screen corroborated purported roles of PLEKHG2 and MED29 as 19q13 amplicon drivers. Most notably, the analysis also revealed novel possible oncogenic functions of nucleoporin NUP153 (ostensibly by modulating TGFbeta signaling) and Kruppel-like transcription factor KLF5 in pancreatic cancer. CONCLUSIONS: By integrating physical and functional genomic data, we were able to simultaneously evaluate many candidate pancreatic cancer genes. Our findings uncover new facets of pancreatic cancer biology, with possible therapeutic implications. More broadly, our study provides a general strategy for the efficient characterization of candidate genes emerging from cancer genome studies.

[356]

TÍTULO / TITLE: - Think Modular: A Simple Apoferritin-Based Platform for the Multifaceted Detection of Pancreatic Cancer.

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

REVISTA / JOURNAL: - ACS Nano. 2013 Aug 29.

●● Enlace al texto completo (gratis o de pago) [1021/nn403465a](#)

AUTORES / AUTHORS: - Hwang MP; Lee JW; Lee KE; Lee KH

INSTITUCIÓN / INSTITUTION: - Center for Biomaterials, Biomedical Research Institute, Korea Institute of Science and Technology (KIS T), 5 Hwarangno 14-gil, Seongbuk-gu, Seoul 136-791, Republic of Korea.

RESUMEN / SUMMARY: - The generation of nanosized probes often requires time-intensive and application-specific optimization processes that involve conjugating a nanoconstruct to a targeting moiety. Herein, we genetically modify apoferritin and generate a universal interface system composed of protein G and 6xHis-tag. The resulting construct, conferred with modularity and high targeting efficiency, is applied toward two distinct applications in the detection of a pancreatic cancer biomarker and used to demonstrate its potential in the facile exchange of nanoprobe components.

[357]

TÍTULO / TITLE: - Assessment of the stromal contribution to Sonic Hedgehog-dependent pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Mol Oncol. 2013 Aug 16. pii: S1574-7891(13)00115-4. doi: 10.1016/j.molonc.2013.08.004.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.molonc.2013.08.004](#)

AUTORES / AUTHORS: - Damhofer H; Medema JP; Veenstra VL; Badea L; Popescu I; Roelink H; Bijlsma MF

INSTITUCIÓN / INSTITUTION: - Laboratory for Experimental Oncology and Radiobiology, Academic Medical Center, University of Amsterdam, Meibergdreef 9, 1105AZ Amsterdam, The Netherlands. Electronic address: h.damhofer@amc.uva.nl.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies. It is typically detected at an advanced stage, at which the therapeutic options are very limited. One remarkable feature of PDAC that contributes to its resilience to treatment is the extreme stromal activation seen in these tumors. Often, the vast majority of tumor bulk consists of non-tumor cells that together provide a tumor-promoting environment. One of the signals that maintains and activates the stroma is the developmental protein Sonic Hedgehog (SHH). As the disease progresses, tumor cells produce increasing amounts of SHH, which activates the surrounding stroma to aid in tumor progression. To better understand this response and identify targets for inhibition, we aimed to elucidate the proteins that mediate the SHH-driven stromal response in PDAC. For this a novel mixed-species coculture model was set up in which the cancer cells are human, and the stroma is modeled by mouse fibroblasts. In conjunction with next-generation sequencing we were able to use the sequence difference between these species to genetically distinguish between the epithelial and stromal responses to SHH. The stromal SHH-dependent genes from this analysis were validated and their relevance for human disease was subsequently determined in two independent patient cohorts. In non-microdissected tissue from PDAC patients, in which a large amount of stroma is present, the targets were confirmed to associate with tumor stroma versus normal pancreatic tissue. Patient survival analysis and immunohistochemistry identified CDA, EDIL3, ITGB4, PLAUR and SPOCK1 as SHH-dependent stromal factors that are

associated with poor prognosis in PDAC patients. Summarizing, the presented data provide insight into the role of the activated stroma in PDAC, and how SHH acts to mediate this response. In addition, the study has yielded several candidates that are interesting therapeutic targets for a disease for which treatment options are still inadequate.

[358]

TÍTULO / TITLE: - The autophagy inhibitor verteporfin moderately enhances the antitumor activity of gemcitabine in a pancreatic ductal adenocarcinoma model.

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

REVISTA / JOURNAL: - J Cancer. 2013 Aug 28;4(7):585-96. doi: 10.7150/jca.7030.

●● Enlace al texto completo (gratis o de pago) [7150/jca.7030](#)

AUTORES / AUTHORS: - Donohue E; Thomas A; Maurer N; Manisali I; Zeisser-Labouebe M; Zisman N; Anderson HJ; Ng SS; Webb M; Bally M; Roberge M

INSTITUCIÓN / INSTITUTION: - 1. Department of Biochemistry and Molecular Biology, University of British Columbia;

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is highly resistant to chemotherapy. It has been described as requiring elevated autophagy for growth and inhibiting autophagy has been proposed as a treatment strategy. To date, all preclinical reports and clinical trials investigating pharmacological inhibition of autophagy have used chloroquine or hydroxychloroquine, which interfere with lysosomal function and block autophagy at a late stage. Verteporfin is a newly discovered autophagy inhibitor that blocks autophagy at an early stage by inhibiting autophagosome formation. Here we report that PDAC cell lines show variable sensitivity to verteporfin in vitro, suggesting cell-line specific autophagy dependence. Using image-based and molecular analyses, we show that verteporfin inhibits autophagy stimulated by gemcitabine, the current standard treatment for PDAC. Pharmacokinetic and efficacy studies in a BxPC-3 xenograft mouse model demonstrated that verteporfin accumulated in tumors at autophagy-inhibiting levels and inhibited autophagy in vivo, but did not reduce tumor volume or increase survival as a single agent. In combination with gemcitabine verteporfin moderately reduced tumor growth and enhanced survival compared to gemcitabine alone. While our results do not uphold the premise that autophagy inhibition might be widely effective against PDAC as a single-modality treatment, they do support autophagy inhibition as an approach to sensitize PDAC to gemcitabine.

[359]

TÍTULO / TITLE: - Targeting pancreatic cancer with magneto-fluorescent theranostic gold nanoshells.

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

REVISTA / JOURNAL: - Nanomedicine (Lond). 2013 Sep 24.

●● Enlace al texto completo (gratis o de pago) [2217/nnm.13.84](#)

AUTORES / AUTHORS: - Chen W; Ayala-Orozco C; Biswal NC; Perez-Torres C; Bartels M; Bardhan R; Stinnet G; Liu XD; Ji B; Deorukhkar A; Brown LV; Guha S; Pautler RG; Krishnan S; Halas NJ; Joshi A

INSTITUCIÓN / INSTITUTION: - Division of Molecular Imaging, Department of Radiology, Baylor College of Medicine, Mail: BCM 360, One Baylor Plaza, Houston, TX 77030, USA and Department of Diagnostic Imaging, The Fourth Hospital of Hebei Medical University/Hebei Province Tumor Hospital, 12 Jiankang Road, Shijiazhuang, Hebei Province 050011, China.

RESUMEN / SUMMARY: - Aim: We report a magneto-fluorescent theranostic nanocomplex targeted to neutrophil gelatinase-associated lipocalin (NGAL) for imaging and therapy of pancreatic cancer. Materials & methods: Gold nanoshells resonant at 810 nm were encapsulated in silica epilayers doped with iron oxide and the near-infrared (NIR) dye indocyanine green, resulting in theranostic gold nanoshells (TGNS), which were subsequently conjugated with antibodies targeting NGAL in AsPC-1-derived xenografts in nude mice. Results: Anti-NGAL-conjugated TGNS specifically targeted pancreatic cancer cells in vitro and in vivo providing contrast for both NIR fluorescence and T2-weighted MRI with higher tumor contrast than can be obtained using long-circulating, but nontargeted, PEGylated nanoparticles. The nanocomplexes also enabled highly specific cancer cell death via NIR photothermal therapy in vitro. Conclusion: TGNS with embedded NIR and magnetic resonance contrasts can be specifically targeted to pancreatic cancer cells with expression of early disease marker NGAL, and enable molecularly targeted imaging and photothermal therapy. Original submitted 6 November 2012; Revised submitted 25 March 2013.

[360]

TÍTULO / TITLE: - MicroRNA-21 in Pancreatic Ductal Adenocarcinoma Tumor-Associated Fibroblasts Promotes Metastasis.

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

REVISTA / JOURNAL: - PLoS One. 2013 Aug 22;8(8):e71978. doi: 10.1371/journal.pone.0071978.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0071978](https://doi.org/10.1371/journal.pone.0071978)

AUTORES / AUTHORS: - Kadera BE; Li L; Toste PA; Wu N; Adams C; Dawson DW; Donahue TR

INSTITUCIÓN / INSTITUTION: - Division of General Surgery, Department of Surgery, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, California, United States of America.

RESUMEN / SUMMARY: - INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) is projected to rise to the second leading cause of U.S. cancer-related deaths by 2020. Novel therapeutic targets are desperately needed. MicroRNAs (miRs) are small noncoding RNAs that function by suppressing gene expression and are dysregulated in cancer. miR-21 is overexpressed in PDAC tumor cells (TC) and is associated with

decreased survival, chemoresistance and invasion. Dysregulation of miR regulatory networks in PDAC tumor-associated fibroblasts (TAFs) have not been previously described. In this study, we show that miR-21 expression in TAFs promotes TC invasion. METHODS: In-situ hybridization for miR-21 was performed on the 153 PDAC patient UCLA tissue microarray and 23 patient-matched lymph node metastases. Stromal and TC histoscores were correlated with clinicopathologic parameters by univariate and multivariate Cox regression. miR-21 positive cells were further characterized by immunofluorescence for mesenchymal/epithelial markers. For in vitro studies, TAFs were isolated from freshly resected human PDAC tumors by the outgrowth method. miR-21 was overexpressed/inhibited in fibroblasts and then co-cultured with GFP-MiaPaCa TCs to assess TC invasion in modified Boyden chambers. RESULTS: miR-21 was upregulated in TAFs of 78% of tumors, and high miR-21 significantly correlated with decreased overall survival (P = 0.04). Stromal miR-21 expression was also significantly associated with lymph node invasion (P = 0.004), suggesting that it is driving TC spread. Co-immunofluorescence revealed that miR-21 colocalized with peritumoral fibroblasts expressing alpha-smooth muscle actin. Moreover, expression of miR-21 in primary TAFs correlated with miR-21 in TAFs from patient-matched LN metastases; evidence that PDAC tumor cells induce TAFs to express miR-21. miR-21 expression in TAFs and TCs promotes invasion of TCs and is inhibited with anti-miR-21. CONCLUSIONS: miR-21 expression in PDAC TAFs is associated with decreased overall survival and promotes TC invasion. Anti-miR-21 may represent a novel therapeutic strategy for dual targeting of both tumor and stroma in PDAC.

[361]

TÍTULO / TITLE: - Pancreatic ductal adenocarcinoma staging.

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

REVISTA / JOURNAL: - Cancer Imaging. 2013 Sep 23;13(3):360-4. doi: 10.1102/1470-7330.2013.9020.

●● Enlace al texto completo (gratis o de pago) 1102/1470-7330.2013.9020

AUTORES / AUTHORS: - Al-Hawary MM; Francis IR

INSTITUCIÓN / INSTITUTION: - Department of Radiology, University of Michigan Health Services, Ann Arbor, MI, USA.

RESUMEN / SUMMARY: - In addition to clinical history and evaluations, the results of laboratory tests and imaging studies help clinicians in determining treatment strategies. Imaging plays a central role in the management of oncology patients including the initial diagnosis, staging, and follow-up to assess treatment response. Historically, radiologists have relied on free-style dictations to convey the results of imaging findings in radiology reports to referring clinicians. These unstructured free-style dictations can potentially be a source of frustration as the pertinent information needed to guide treatment may be omitted or difficult to extract from the report,

thereby limiting its completeness and usefulness. These limitations can be overcome by adopting a structured and reproducible form of reporting imaging studies to help clinicians in deciding the best treatment strategy for each patient. There is a growing need to establish standardized radiology reporting templates for specific disease processes. One such example involves patients with pancreatic ductal adenocarcinoma, as imaging findings determine the treatment arm to which the patient is assigned. In this presentation, we outline a list of essential features that need to be included in a structured report and highlight this with illustrative case examples.

[362]

TÍTULO / TITLE: - Is there a proper type of management for branch-duct intraductal papillary mucinous tumors of the pancreas?

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

REVISTA / JOURNAL: - JOP. 2013 Sep 10;14(5):525-7. doi: 10.6092/1590-8577/1895.

AUTORES / AUTHORS: - Casadei R; Ricci C; Minni F

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[363]

TÍTULO / TITLE: - New morphological features for grading pancreatic ductal adenocarcinomas.

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

REVISTA / JOURNAL: - Biomed Res Int. 2013;2013:175271. doi: 10.1155/2013/175271. Epub 2013 Jul 25.

●● Enlace al texto completo (gratis o de pago) [1155/2013/175271](#)

AUTORES / AUTHORS: - Song JW; Lee JH

INSTITUCIÓN / INSTITUTION: - Department of Computer & Information Engineering, Inha University, 253 Yonghyun-dong, Nam-gu, Incheon 402-751, Republic of Korea.

RESUMEN / SUMMARY: - Pathological diagnosis is influenced by subjective factors such as the individual experience and knowledge of doctors. Therefore, it may be interpreted in different ways for the same symptoms. The appearance of digital pathology has created good foundation for objective diagnoses based on quantitative feature analysis. Recently, numerous studies are being done to develop automated diagnosis based on the digital pathology. But there are as of yet no general automated methods for pathological diagnosis due to its specific nature. Therefore, specific methods according to a type of disease and a lesion could be designed. This study proposes quantitative features that are designed to diagnose pancreatic ductal adenocarcinomas. In the diagnosis of pancreatic ductal adenocarcinomas, the region of interest is a duct that consists of lumen and epithelium. Therefore, we first segment the lumen and epithelial nuclei from a tissue image. Then, we extract the specific

features to diagnose the pancreatic ductal adenocarcinoma from the segmented objects. The experiment evaluated the classification performance of the SVM learned by the proposed features. The results showed an accuracy of 94.38% in the experiment distinguishing between pancreatic ductal adenocarcinomas and normal tissue and a classification accuracy of 77.03% distinguishing between the stages of pancreatic ductal adenocarcinomas.

[364]

TÍTULO / TITLE: - Advancements in pancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - Expert Rev Gastroenterol Hepatol. 2013 Jul;7(5):477-90. doi: 10.1586/17474124.2013.811058.

●● Enlace al texto completo (gratis o de pago) [1586/17474124.2013.811058](#)

AUTORES / AUTHORS: - Sadaria MR; Hruban RH; Edil BH

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Colorado Anschutz Medical Campus, Division of GI, Tumor and Endocrine Surgery, Academic Office One, 12631 East 17th Avenue, C311, Aurora, CO 80045, USA.

RESUMEN / SUMMARY: - Pancreatic neuroendocrine tumors (PanNETs) have increased in incidence in the USA over the last 20 years. Although PanNETs are often misconceived as being indolent tumors as they have a far more favorable prognosis over pancreatic adenocarcinoma, roughly 60-70% of patients have metastatic disease at the time of diagnosis due to presentation late in the disease process. While improvements in imaging modalities allow for early detection and better tumor localization, recent advancements in basic science, as well as surgical and medical management of PanNETs have further improved the prognosis. The mainstay of therapy for localized PanNETs is surgical intervention, which has become safer and is slowly shifting towards a more minimally invasive approach. However, the prognosis still remains relatively bleak for patients with unresectable disease. Fortunately, novel molecular targeted therapies, such as everolimus and sunitinib, have recently come into the limelight and have shown significant promise for the treatment of locally advanced and metastatic disease.
