#01#

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

Pancreatic cancer.

Julio - Agosto 2013 / July - August 2013

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[1]

TÍTULO / TITLE: - Successful everolimus treatment in a patient with advanced pancreatic neuroendocrine tumor who developed everolimus-induced interstitial lung disease on two occasions: a case report.

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

REVISTA / JOURNAL: - Chemotherapy. 2013;59(1):74-8. doi: 10.1159/000351103. Epub 2013 Jul 18.

●● Enlace al texto completo (gratuito o de pago) 1159/000351103

AUTORES / AUTHORS: - Nakayama Y; Ikeda M; Kojima M; Goto K; Hara M; Okuyama H; Takahashi H; Ohno I; Shimizu S; Mitsunaga S; Okusaka T

INSTITUCIÓN / INSTITUTION: - Division of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East, Kashiwa, Japan.

RESUMEN / SUMMARY: - Chemotherapy-associated interstitial lung disease (ILD) is often fatal, and the chemotherapeutic regimen generally cannot be resumed. ILD associated with the mammalian target of rapamycin (mTOR) inhibitor everolimus has many features distinct from chemotherapy-associated ILD. We present the case of a 58-year-old woman with an advanced pancreatic neuroendocrine tumor with liver metastases, in whom everolimus treatment was maintained and resulted in a partial response despite two occurrences of everolimus-induced ILD during a 31-month treatment period until disease progression. Physicians treating with everolimus should monitor patients closely for ILD and should apply appropriate management strategies to optimize the possibility of maintaining everolimus therapy. © 2013 S. Karger AG, Basel.

TÍTULO / TITLE: - REG3beta DEFICIENCY IMPAIRS PANCREATIC TUMOR GROWTH BY SKEWING MACROPHAGE POLARIZATION.

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

REVISTA / JOURNAL: - Cancer Res. 2013 Jul 18.

●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-12-3057

AUTORES / AUTHORS: - Gironella M; Calvo C; Fernandez A; Closa D; Iovanna JL; Rosello-Catafau J; Folch-Puy E

INSTITUCIÓN / INSTITUTION: - Gastroenterology, Hospital Clinic of Barcelona/CIBERehd.

RESUMEN / SUMMARY: - The lectin Reg3beta provides crucial protection to various tissues against inflammation, a potential risk factor for pancreatic ductal adenocarcinoma. Reg3beta is also overexpressed in serum and pancreatic juice from patients with this cancer but its function in this context remains to be elucidated. In this study, we investigated the role of Reg3beta in tumor development in an orthotopic mouse model of pancreatic cancer. Reg3beta deletion in mice drastically impaired pancreatic tumor growth correlating with decreased angiogenesis and increased apoptosis of tumor cells. Moreover, Reg3beta deficiency resulted in an alteration of the tumoral immune microenvironment, reflected by a decrease in the M2/M1 ratio concerning tumor-associated macrophages (TAM) and an up-regulation of CD3+ cell infiltration. Addition of Reg3beta to pre-stimulated RAW 264.7 or primary macrophages enhanced M2 polarization through the activation of STAT3 signaling pathway. Conditioned media from Reg3beta-M2-polarized primary macrophages inhibited apoptosis and prolonged the viability of Panc02 tumor cells. Our studies reveal a novel role for Reg3beta as a tumor promoter in pancreatic adenocarcinoma through the regulation of tumor stroma. Thus, inhibition of this protein may be a useful strategy in treatment of pancreatic cancer.

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[2]

TÍTULO / TITLE: - Adenovirus vector-mediated Gli1 siRNA induces growth inhibition and apoptosis in human pancreatic cancer with Smo-dependent or Smo-independent Hh pathway activation in vitro and in vivo.

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

REVISTA / JOURNAL: - Cancer Lett. 2013 Jun 18. pii: S0304-3835(13)00460-6. doi: 10.1016/j.canlet.2013.06.010.

●● Enlace al texto completo (gratuito o de pago) 1016/j.canlet.2013.06.010

AUTORES / AUTHORS: - Guo J; Gao J; Li Z; Gong Y; Man X; Jin J; Wu H

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Changhai Hospital, Second Military Medical University, Shanghai 200433, China.
RESUMEN / SUMMARY: - Activation of Hedgehog (Hh) signaling pathway is a core molecular mechanism in pancreatic carcinogenesis. However, the inhibition of upstream Hh signals does not inhibit the growth of a subset of pancreatic cancer (PC). This study was to examine the effect of siRNA targeting Gli1, the downstream component of Hh pathway, on PC cells and to provide some insight into the underlying mechanisms. A Gli1siRNA-expressing adenovirus (Ad-U6-Gli1siRNA) was constructed, and its effect on PC cells was investigated in vitro and in vivo. Gli1 was expressed in 83.3% (20/24) PC tissues, whereas no expression was found in normal pancreatic ductal epithelium. Gli1 was expressed in SW1990 and CFPAC cells in which Smo was completely absent, as well as in PaTu8988, Panc-1 and BxPC-3 cells in which Smo was concomitantly present. Ad-U6-Gli1siRNA induced cell growth inhibition, strong G0/G1 cell cycle arrest and apoptosis in all five human PC cell lines. Meanwhile, Ad-U6-Gli1siRNA significantly suppressed the expression of Gli1, Ptch1 and two target genes, Cyclin D2 and Bcl-2, in all five lines. Furthermore, two tumor xenograft nude mice models were established by subcutaneously injecting Smo-positive Panc-1 cells or Smo-negative SW1990 cells. The in vivo experimental results demonstrated that Ad-U6-Gli1siRNA inhibited the growth of both Panc1-derived and SW1990-derived tumors and induced cell apoptosis. Our study indicates that Gli1-targeting siRNA could induce growth inhibition and apoptosis in PC through knockdown of Gli1 and its target genes; and this method may represent a more effective therapeutic strategy for PC with Smo-dependent or Smo-independent Hh pathway activation.

TÍTULO / TITLE: - Detection of Pancreatic Ductal Adenocarcinoma in Mice by Ultrasound Imaging of Thymocyte Differentiation Antigen 1.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Gastroenterology. 2013 Jun 18. pii: S0016-5085(13)00913-X. doi: 10.1053/j.gastro.2013.06.011.
●● Enlace al texto completo (gratuito o de pago)
1053/j.gastro.2013.06.011
AUTORES / AUTHORS: - Foygel K; Wang H; Machtaler S; Lutz AM; Chen R; Pysz M; Lowe AW; Tian L; Carrigan T; Brentnall TA; Willmann JK
INSTITUCIÓN / INSTITUTION: - Department of Radiology, Molecular Imaging Program at Stanford (MIPS); Stanford University, Stanford, California, USA.
RESUMEN / SUMMARY: - BACKGROUND & AIMS: Early detection of pancreatic ductal adenocarcinoma (PDAC) allows for surgical resection and increases patient survival times. Imaging agents that bind and amplify the signal of neovascular proteins in neoplasms can be detected by ultrasound, enabling accurate detection of small lesions. We searched for new markers of

neovasculature in PDAC and assessed their potential for tumor detection by ultrasound molecular imaging. METHODS: Thymocyte Differentiation Antigen 1 (Thy1) was identified as a specific biomarker of PDAC neovasculature by proteomic analysis. Upregulation in PDAC was validated by immunohistochemical analysis of pancreatic tissue samples from 28 healthy individuals, 15 with primary chronic pancreatitis tissues, and 196 with PDAC. Binding of Thy1-targeted contrast microbubbles was assessed in cultured cells, in mice with orthotopic PDAC xenograft tumors expressing human Thy1 on the neovasculature, and on the neovasculature of a genetic mouse model of PDAC. RESULTS: Based on immunohistochemical analyses, levels of Thy1 were significantly higher in the vascular of human PDAC than chronic pancreatitis (P=.007) or normal tissue samples (P<.0001). In mice, ultrasound imaging accurately detected human Thy1-positive PDAC xenografts, as well as PDACs that express endogenous Thy1 in genetic mouse models of PDAC. CONCLUSION: We have identified and validated Thy1 as a marker of PDAC that can be detected by ultrasound molecular imaging in mice. The development of a specific imaging agent and identification of Thy1 as a new biomarker could aid in the diagnosis of this cancer and management of patients.

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[3]

TÍTULO / TITLE: - Specific glycoforms of MUC5AC and endorepellin accurately distinguish mucinous from non-mucinous pancreatic cysts.

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

REVISTA / JOURNAL: - Mol Cell Proteomics. 2013 Jul 8.

●● Enlace al texto completo (gratuito o de pago) 1074/mcp.M113.030700

AUTORES / AUTHORS: - Cao Z; Maupin K; Curnutte B; Fallon B; Feasley CL; Brouhard E; Kwon R; West CM; Cunningham J; Brand R; Castelli P; Crippa S; Feng Z; Allen P; Simeone DM; Haab BB

INSTITUCIÓN / INSTITUTION: - Van Andel Research Institute, United States;

RESUMEN / SUMMARY: - Purpose: Previously we have shown that specific protein glycoforms may be uniquely informative about the pathological state of a cyst and may serve as accurate biomarkers. Here we tested this hypothesis using antibody-lectin sandwich arrays in broad screens of protein glycoforms and in targeted studies of candidate markers. Experimental design: We profiled 16 different glycoforms of proteins captured by 72 different antibodies in cyst fluid from mucinous and non-mucinous cysts (n = 22), and we then tested a three marker panel in 22 addition samples and 22 blinded samples. Results: Glycan alterations were not widespread among the proteins but were mainly confined to MUC5AC and endorepellin. Specific glycoforms of these proteins, defined by reactivity with wheat-germ agglutinin (WGA) and a blood group H (BGH) antibody, were significantly elevated in mucinous cysts, whereas the core protein levels were not significantly elevated. A three-marker panel based on these glycoforms distinguished mucinous from non-mucinous cysts with 93%

accuracy (89% sensitivity, 100% specificity) in a pre-validation sample set (n = 44) and with 91% accuracy (87% sensitivity, 100% specificity) in independent, blinded samples (n = 22). Targeted lectin measurements and mass spectrometry analyses indicated that the higher WGA and BGH reactivity was due to oligosaccharides terminating in GlcNAc or N-acetyl-lactosamine with occasional alpha1,2-linked fucose. Conclusions: MUC5AC and endorepellin glycoforms may be highly specific and sensitive biomarkers for the differentiation of mucinous from non-mucinous pancreatic cysts.

TÍTULO / TITLE: - CTGF antagonism with mAb FG-3019 enhances chemotherapy response without increasing drug delivery in murine ductal pancreas cancer.

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

REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Jul 23;110(30):12325-30. doi: 10.1073/pnas.1300415110. Epub 2013 Jul 8.

●● Enlace al texto completo (gratuito o de pago) 1073/pnas.1300415110

AUTORES / AUTHORS: - Neesse A; Frese KK; Bapiro TE; Nakagawa T; Sternlicht MD; Seeley TW; Pilarsky C; Jodrell DI; Spong SM; Tuveson DA

INSTITUCIÓN / INSTITUTION: - Cancer Research UK Cambridge Institute, University of Cambridge, Cambridge CB2 0RE, United Kingdom.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDA) is characterized by abundant desmoplasia and poor tissue perfusion. These features are proposed to limit the access of therapies to neoplastic cells and blunt treatment efficacy. Indeed, several agents that target the PDA tumor microenvironment promote concomitant chemotherapy delivery and increased antineoplastic response in murine models of PDA. Prior studies could not determine whether chemotherapy delivery or microenvironment modulation per se were the dominant features in treatment response, and such information could guide the optimal translation of these preclinical findings to patients. To distinguish between these possibilities, we used a chemical inhibitor of cytidine deaminase to stabilize and thereby artificially elevate gemcitabine levels in murine PDA tumors without disrupting the tumor microenvironment. Additionally, we used the FG-3019 monoclonal antibody (mAb) that is directed against the pleiotropic matricellular signaling protein connective tissue growth factor (CTGF/CCN2). Inhibition of cytidine deaminase raised the levels of activated gemcitabine within PDA tumors without stimulating neoplastic cell killing or decreasing the growth of tumors, whereas FG-3019 increased PDA cell killing and led to a dramatic tumor response without altering gemcitabine delivery. The response to FG-3019 correlated with the decreased expression of a previously described promoter of PDA chemotherapy resistance, the X-linked inhibitor of apoptosis protein. Therefore, alterations in survival cues following targeting of tumor microenvironmental factors may play an important role in treatment responses in animal models, and by extension in PDA patients.

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[4]

TÍTULO / TITLE: - The value of gadoxetic acid-enhanced and diffusion-weighted MRI for prediction of grading of pancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - Acta Radiol. 2013 Jul 29.

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

1177/0284185113494982

AUTORES / AUTHORS: - Jang KM; Kim SH; Lee SJ; Choi D

INSTITUCIÓN / INSTITUTION: - Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea.

RESUMEN / SUMMARY: - BACKGROUND: Parenchyma-preserving resection for the treatment of benign pancreatic neuroendocrine tumors (NETs) has been tried, and preoperative prediction of benign pancreatic NET is important. Recently, diffusion-weighted imaging (DWI) of abdomen magnetic resonance imaging (MRI) has been used to characterize benign and malignant tumors and DWI might be helpful in prediction of benign pancreatic NETs. PURPOSE: To evaluate the value of gadoxetic acid-enhanced MRI and DWI in predicting benign pancreatic NETs for determination of parenchyma-preserving resection. MATERIAL AND METHODS: Our ethics committee approved this study with a waiver of informed consent given its retrospective design. We searched radiology and pathology databases from November 2010 to July 2012 to identify patients who underwent surgery for pancreatic NETs (<4 cm). Twenty patients in the benign group and 14 patients in the non-benign group were included in this study. Two radiologists analyzed the morphologic features, signal intensity on MR images including DWI (b = 800), and dynamic enhancement pattern of the tumors with consensus. The tumor-to-parenchyma ratio and tumor apparent diffusion coefficients (ADCs) were quantitatively assessed. RESULTS: The benign pancreatic NETs were more often round (7/20, 35%) or ovoid (13/20, 65%) in shape and less hypovascular on the arterial phase (3/20, 15%) than were the non-benign pancreatic NETs (1/14, 7.1% and 5/14, 35.8%; 7/14, 50% respectively; P < 0.05). Main pancreatic duct dilatation by tumors was demonstrated only in non-benign pancreatic NETs (4/14, 28.4%; P = 0.021). ADC values and ratios were significantly different between benign pancreatic NETs (mean, 1.48 x 10-3 mm2/sec, 1.11 +/- 0.25, each) and non-benign pancreatic NETs (mean, 1.04 x 10-3 mm2/sec, 0.74 +/- 0.13, each) (P < 0.01). Other qualitative and quantitative analyses between benign and non-benign pancreatic NETs were not significantly different (P > 0.05). CONCLUSION: Abdominal MRI with DWI may be useful for differentiating benign pancreatic NETs from non-benign pancreatic NETs, which might be helpful for determination of parenchyma-preserving resection.

TÍTULO / TITLE: - Migratory Activity of CD105+ Pancreatic Cancer Cells Is Strongly Enhanced by Pancreatic Stellate Cells.

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

REVISTA / JOURNAL: - Pancreas. 2013 Jul 26.

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

1097/MPA.0b013e318293e7bd

AUTORES / AUTHORS: - Fujiwara K; Ohuchida K; Ohtsuka T; Mizumoto K; Shindo K; Ikenaga N; Cui L; Takahata S; Aishima S; Tanaka M

INSTITUCIÓN / INSTITUTION: - From the *Departments of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, Fukuoka; daggerResearch Fellow of the Japan Society for the Promotion of Science, Tokyo; double daggerAdvanced Medical Initiatives, Graduate School of Medical Sciences, Kyushu University, Fukuoka; section signKyushu University Hospital Cancer Center, Fukuoka; parallelDepartment of Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University, Fukuoka; paragraph signPostdoctoral Fellow for Research Abroad, Tokyo, Japan; and #Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA.

RESUMEN / SUMMARY: - OBJECTIVES: CD105 expression correlates with prognosis for several cancers. However, its significance in pancreatic cancer is unclear. METHODS: We analyzed CD105 expression in resected pancreatic cancer tissue and pancreatic cancer cell lines, compared the properties of CD105 and CD105 cells using quantitative RT-PCR and migration assays, and evaluated the relationship between CD105 cells and pancreatic stellate cells (PSCs). RESULTS: Immunohistochemistry showed that the frequency of CD105 expression was higher in pancreatic cancer than that in normal tissue (8% vs 0%, respectively). In flow cytometry, CD105 was expressed in pancreatic cancer cells, whereas weak CD105 expression was detected in normal pancreatic ductal epithelial cells. Quantitative RT-PCR showed that E-cadherin mRNA expression was suppressed and vimentin mRNA was overexpressed in CD105 cells ($P < 0.05$). Migration of CD105 cancer cells was strongly enhanced (more than that of CD105 cells) in coculture with PSCs ($P < 0.05$). CD105 expression did not correlate to clinicopathologic characteristics or the Kaplan-Meier survival analysis. CONCLUSIONS: Suppression of an epithelial marker and overexpression of a mesenchymal marker suggest that epithelial-mesenchymal transition is induced in CD105 pancreatic cancer cells. CD105 pancreatic cancer cell migration is strongly enhanced by PSCs, suggesting that these cells play a role in the pancreatic cancer microenvironment.

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[5]

TÍTULO / TITLE: - Viscum album [L.] extract therapy in patients with locally advanced or metastatic pancreatic cancer: A randomised clinical trial on overall survival.

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

REVISTA / JOURNAL: - Eur J Cancer. 2013 Jul 24. pii: S0959-8049(13)00550-9. doi: 10.1016/j.ejca.2013.06.043.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ejca.2013.06.043

AUTORES / AUTHORS: - Troger W; Galun D; Reif M; Schumann A; Stankovic N; Milicevic M

INSTITUCIÓN / INSTITUTION: - Clinical Research Dr. Troger, Freiburg, Germany. Electronic address: troeger@crdt.de.

RESUMEN / SUMMARY: - BACKGROUND: The unfavourable side-effects of late-stage pancreatic cancer treatments call for non-toxic and effective therapeutic approaches. We compared the overall survival (OS) of patients receiving an extract of Viscum album [L.] (VaL) or no antineoplastic therapy. METHODS: This is a prospective, parallel, open label, monocentre, group-sequential, randomised phase III study. Patients with locally advanced or metastatic cancer of the pancreas were stratified according to a binary prognosis index, composed of tumour stage, age and performance status; and were evenly randomised to subcutaneous injections of VaL extracts or no antineoplastic therapy (control). VaL was applied in a dose-escalating manner from 0.01mg up to 10mg three times per week. Patients in both groups received best supportive care. The primary end-point was 12-month OS, assessed in a group-sequential analysis. FINDINGS: We present the first interim analysis, including data from 220 patients. Baseline characteristics were well balanced between the study arms. Median OS was 4.8 for VaL and 2.7months for control patients (prognosis-adjusted hazard ratio, HR=0.49; p<0.0001). Within the 'good' prognosis subgroup, median OS was 6.6 versus 3.2months (HR=0.43; p<0.0001), within the 'poor' prognosis subgroup, it was 3.4 versus 2.0months respectively (HR=0.55; p=0.0031). No VaL-related adverse events were observed. CONCLUSION: VaL therapy showed a significant and clinically relevant prolongation of OS. The study findings suggest VaL to be a non-toxic and effective second-line therapy that offers a prolongation of OS as well as less disease-related symptoms for patients with locally advanced or metastatic pancreatic cancer.

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[6]

TÍTULO / TITLE: - Equal Efficacy of Endoscopic and Surgical Cystogastrostomy for Pancreatic Pseudocyst Drainage in a Randomized Trial.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 May 31. pii: S0016-5085(13)00844-5. doi: 10.1053/j.gastro.2013.05.046.

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

1053/j.gastro.2013.05.046

AUTORES / AUTHORS: - Varadarajulu S; Bang JY; Sutton BS; Trevino JM; Christein JD; Wilcox CM

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology-Hepatology, University of Alabama at Birmingham, Birmingham, Alabama. Electronic address: svaradarajulu@yahoo.com.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Although surgery is the standard technique for drainage of pancreatic pseudocysts, use of endoscopic methods is increasing. We performed a single-center, open-label, randomized trial to compare endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage. METHODS: Patients with pancreatic pseudocysts underwent endoscopic (n = 20) or surgical cystogastrostomy (n = 20). The primary end point was pseudocyst recurrence after a 24-month follow-up period. Secondary end points were treatment success or failure, complications, re-interventions, length of hospital stay, physical and mental health scores, and total costs. RESULTS: At the end of the follow-up period, none of the patients who received endoscopic therapy had a pseudocyst recurrence, compared with 1 patient treated surgically. There were no differences in treatment successes, complications, or re-interventions between the groups. However, the length of hospital stay was shorter for patients who underwent endoscopic cystogastrostomy (median, 2 days, vs 6 days in the surgery group; P < .001). Although there were no differences in physical component scores and mental health component scores (MCS) between groups at baseline on the Medical Outcomes Study 36-Item Short-Form General Survey questionnaire, longitudinal analysis showed significantly better physical component scores (P = .019) and mental health component scores (P = .025) for the endoscopy treatment group. The total mean cost was lower for patients managed by endoscopy than surgery ($7011 vs $15,052; P = .003). CONCLUSIONS: In a randomized trial comparing endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage, none of the patients in the endoscopy group had pseudocyst recurrence during the follow-up period, therefore there is no evidence that surgical cystogastrostomy is superior. However, endoscopic treatment was associated with shorter hospital stays, better physical and mental health of patients, and lower cost. Trial Registration: ClinicalTrials.gov: NCT00826501.

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[7]

TÍTULO / TITLE: - Multicenter phase II trial to investigate safety and efficacy of gemcitabine combined with cetuximab as adjuvant therapy in pancreatic cancer (ATIP).

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

REVISTA / JOURNAL: - Ann Oncol. 2013 Jul 29.

●● Enlace al texto completo (gratuito o de pago) 1093/annonc/mdt270

AUTORES / AUTHORS: - Fensterer H; Schade-Brittinger C; Muller HH; Tebbe S; Fass J; Lindig U; Settmacher U; Schmidt WE; Marten A; Ebert MP; Kornmann M; Hofheinz R; Endlicher E; Brendel C; Barth PJ; Bartsch DK; Michl P; Gress TM

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology.

RESUMEN / SUMMARY: - BACKGROUND: To investigate whether addition of cetuximab to standard adjuvant chemotherapy with gemcitabine improves outcome in pancreatic cancer, specifically whether the rate of disease-free survival (DFS) at 18 months (primary end point) exceeds the previously reported 35% of gemcitabine alone. PATIENTS AND METHODS: Prospective, open-label, multicenter, nonrandomized phase II study in 76 patients with R0- or R1-resected ductal adenocarcinoma of the pancreas included between October 2006 and November 2008. Gemcitabine and cetuximab were administered for 24 weeks. Secondary end points included overall survival (OS) and toxic effect. RESULTS: Seventy-three patients received cetuximab. Median DFS was 10.0 [95% confidence interval (CI) 8.9-13.6] months and the DFS rate at month 18 of 27.1% (16.7%-37.6%) was inferior to 35%. Median OS was 22.4 (18.2-27.9) months. Subgroup analyses revealed a nonsignificant increase in DFS for patients with versus without skin toxic effect >/=grade 2 (median 14.7 versus 8.3 months, P = 0.073) and wild-type versus mutated K-Ras (median 11.5 versus 9.3 months, P = 0.57). Grade ¾ toxic effects included neutropenia (11.0%), thrombopenia (7%), skin toxic effect (7%) and allergic reactions (7%). CONCLUSION: Addition of cetuximab to adjuvant gemcitabine does not seem to improve DFS or OS of unstratified pancreatic cancer patients. Trends for improved DFS in patients with wild-type K-Ras and skin toxic effect remain to be confirmed.

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[8]

TÍTULO / TITLE: - Targeted therapy of spontaneous murine pancreatic tumors by polymeric micelles prolongs survival and prevents peritoneal metastasis.

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

REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Jul 9;110(28):11397-402. doi: 10.1073/pnas.1301348110. Epub 2013 Jun 25.

●● Enlace al texto completo (gratuito o de pago) 1073/pnas.1301348110

AUTORES / AUTHORS: - Cabral H; Murakami M; Hojo H; Terada Y; Kano MR; Chung UI; Nishiyama N; Kataoka K

INSTITUCIÓN / INSTITUTION: - Departments of Bioengineering and Materials Engineering, Graduate School of Engineering, University of Tokyo, Bunkyo-ku, Tokyo 113-8656, Japan.

RESUMEN / SUMMARY: - Nanoscaled drug-loaded carriers are of particular interest for efficient tumor therapy as numerous studies have shown improved targeting and efficacy. Nevertheless, most of these studies have been

performed against allograft and xenograft tumor models, which have altered microenvironment features affecting the accumulation and penetration of nanocarriers. Conversely, the evaluation of nanocarriers on genetically engineered mice, which can gradually develop clinically relevant tumors, permits the validation of their design under normal processes of immunity, angiogenesis, and inflammation. Therefore, considering the poor prognosis of pancreatic cancer, we used the elastase 1-promoted luciferase and Simian virus 40 T and t antigens transgenic mice, which develop spontaneous bioluminescent pancreatic carcinoma, and showed that long circulating micellar nanocarriers, incorporating the parent complex of oxaliplatin, inhibited the tumor growth as a result of their efficient accumulation and penetration in the tumors. The reduction of the photon flux from the endogenous tumor by the micelles correlated with the decrease of serum carbohydrate-associated antigen 19-9 marker. Micelles also reduced the incidence of metastasis and ascites, extending the survival of the transgenic mice.

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[9]

TÍTULO / TITLE: - Natural history and malignant risk factors of solid pseudopapillary tumors of the pancreas.

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

REVISTA / JOURNAL: - Postgrad Med. 2013 Mar;125(2):92-9. doi: 10.3810/pgm.2013.03.2634.

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

3810/pgm.2013.03.2634

AUTORES / AUTHORS: - Park JK; Cho EJ; Ryu JK; Kim YT; Yoon YB

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea. mdsophie@gmail.com.

RESUMEN / SUMMARY: - Background and Aim: Solid pseudopapillary tumors (SPTs) of the pancreas are unusual neoplasms of uncertain prognosis. Most patients with SPTs have a good prognosis after undergoing surgical resection, but there are rare cases in which a locally infiltrative growth pattern and metastatic variety are exhibited, or recurrence of the disease after surgery occurs; these cases have been reported with very poor clinical outcomes. Our study investigated the natural history of SPTs and delineated the clinicopathologic features that may predict the malignancy potential of the disease. Methods: A total of 100 patients with suspected SPTs were enrolled in our study and 77 patients underwent surgical resection. A resulting 60 tumors were pathologically proven to be SPTs and the affected patients were followed-up regularly after surgery. Clinical and pathologic data for all 100 patients were analyzed. Results: Of the 60 total patients with histologically positive SPTs, 55 (92%) were women and 5 (8%) were men. The median patient age was 34 years (range, 13-77 years). Among the 60 patients, 9 had malignant SPTs and

51 had benign SPTs. Deep parenchymal invasion into the surrounding tissue was the most frequent pathologic feature suggesting malignancy (75%) among the 60 patients who underwent surgical resection. Patient clinicopathologic characteristics and demographic factors were compared between those who had benign SPTs and those who had malignant SPTs. There were no significant differences in the various patient features between the 2 groups, including age, sex, symptoms, tumor size, tumor location, internal tumor composition, pattern of tumor calcification, tumor necrosis, hemorrhage, and immunohistochemical tumor tissue patterns. There were 2 patients who had distant metastasis; 1 presented with distal metastasis in the liver and the other patient had recurrence of cancer with a peritoneal mass after surgery. Metastasectomy was performed on the 2 patients and there was no mortality or disease progression during the follow-up period (median, 143 months; range, 53-319 months). Conclusion: Solid pseudopapillary tumors are low-grade tumors that have a generally good prognosis. However, the clinical development and malignancy potential of SPTs are neither fully understood nor predictable, even with histologically benign tumors. Further investigations in tumor biology, along with long-term patient follow-up, may provide insight into the disease process and clinical development of SPTs.

TÍTULO / TITLE: - A patient with situs inversus totalis and pancreatic head cancer.

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

REVISTA / JOURNAL: - Dig Liver Dis. 2013 Jun 28. pii: S1590-8658(13)00054-6. doi: 10.1016/j.dld.2013.02.003.

●● Enlace al texto completo (gratuito o de pago) 1016/j.dld.2013.02.003

AUTORES / AUTHORS: - Zheng Z; Xiao Y; Zhang S; Pu G

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, The Third People's Hospital of Chengdu, The Second Affiliated Hospital of Chengdu, Chongqing Medical University, Chengdu, Sichuan Province, China.

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[10]

TÍTULO / TITLE: - A case report of a patient with advanced acinar cell carcinoma of the pancreas: long-term survival with regional, systemic and targeted therapy.

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

REVISTA / JOURNAL: - Tumori. 2013 Mar-Apr;99(2):e61-4. doi: 10.1700/1283.14209.

●● Enlace al texto completo (gratuito o de pago) 1700/1283.14209

AUTORES / AUTHORS: - Ang C; Herran LA; Lagunes DR; Klimstra DS; Kemeny NE

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Gastrointestinal Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA.
RESUMEN / SUMMARY: - Acinar cell carcinoma of the pancreas is an uncommon malignancy for which there are no prospective, randomized data to guide therapy. We describe the clinical course and management of a patient with advanced pancreatic acinar cell carcinoma who is alive seven years after diagnosis using systemic and regional chemotherapies as well as molecularly targeted agents.

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[11]
TÍTULO / TITLE: - Safety, tolerability, pharmacokinetics, and pharmacodynamics of a long-acting release (LAR) formulation of pasireotide (SOM230) in patients with gastroenteropancreatic neuroendocrine tumors: results from a randomized, multicenter, open-label, phase I study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Aug;72(2):387-95. doi: 10.1007/s00280-013-2202-1. Epub 2013 Jun 14.
●● Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2202-1
AUTORES / AUTHORS: - Wolin EM; Hu K; Hughes G; Bouillaud E; Giannone V; Resendiz KH
INSTITUCIÓN / INSTITUTION: - Carcinoid/Neuroendocrine Tumor Program, Samuel Oschin Cancer Center, Cedars-Sinai Medical Center, 8700 Beverly Boulevard, Los Angeles, CA, 90048, USA, edward.wolin@cshs.org.
RESUMEN / SUMMARY: - PURPOSE: Pasireotide (SOM230), a novel multireceptor ligand somatostatin analog (SSA), binds with high affinity to four of the five somatostatin receptor subtypes (sst1-3, 5). This study evaluated the safety, tolerability, pharmacokinetics, and pharmacodynamics profiles of pasireotide long-acting release (LAR) formulation in patients with advanced gastroenteropancreatic neuroendocrine tumor (GEP NET) refractory to other SSAs. METHODS: In this randomized, multicenter, open-label, phase II study, patients with biopsy-proven primary or metastatic GEP NET refractory to available SSAs were randomly assigned 1:1:1 to receive pasireotide LAR by deep intragluteal injection at a dose of 20, 40, or 60 mg once every 28 days for 3 months. RESULTS: Forty-two patients received pasireotide LAR. Adverse events were reported by 34 (81 %) patients, with the most frequently reported including diarrhea, fatigue, abdominal pain, and nausea. Mean fasting glucose levels were increased compared with baseline at all points throughout the study. After the third injection of pasireotide LAR, the median trough plasma concentrations on day 84 were 4.82, 12.0, and 19.7 ng/mL in the 20-, 40-, and 60-mg treatment groups, respectively. Drug accumulation was limited for each dose based on the increase in trough concentrations after the first to third injections (accumulation ratios were approximately 1 from all dose levels).

CONCLUSIONS: This study demonstrated that a new, once-monthly, intramuscular LAR formulation of pasireotide was well tolerated in patients with advanced GEP NET. Steady state levels of plasma pasireotide were achieved after three injections.

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[12]

TÍTULO / TITLE: - Putative Predictive Biomarkers of Survival in Patients with Metastatic Pancreatic Adenocarcinoma Treated with Gemcitabine and Ganitumab, an IGF1R Inhibitor.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Aug 1;19(15):4282-9. doi: 10.1158/1078-0432.CCR-12-1840. Epub 2013 Jun 5.

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-12-1840

AUTORES / AUTHORS: - McCaffery I; Tudor Y; Deng H; Tang R; Suzuki S; Badola S; Kindler HL; Fuchs CS; Loh E; Patterson SD; Chen L; Gansert JL

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Amgen Inc., Thousand Oaks; Amgen Inc., South San Francisco, California; Amgen Inc., Cambridge; Dana-Farber Cancer Institute, Boston, Massachusetts; and University of Chicago Medical Center, Chicago, Illinois.

RESUMEN / SUMMARY: - PURPOSE: This planned exploratory analysis assessed the predictive nature of baseline circulating factors of the insulin-like growth factor (IGF) axis on the treatment effect of ganitumab (monoclonal antibody inhibitor of IGF-1 receptor) plus gemcitabine in a randomized phase II study in metastatic pancreatic adenocarcinoma. EXPERIMENTAL DESIGN: Baseline levels of IGFs/IGF binding proteins (IGFBP) were analyzed in serum or plasma. Mutations and gene expression were analyzed in archival samples. Treatment effects between biomarker subgroups were compared for overall survival (OS). Associations of tumor markers with OS were evaluated. RESULTS: For patients with evaluable samples, ganitumab was associated with improved OS versus placebo (HR, 0.49; 95% CI: 0.28-0.87). The treatment effect on improved OS was strong in the patient subset with higher levels of IGF-1, IGF-2, or IGFBP-3, or lower levels of IGFBP-2, but not so on the other corresponding subset. Median OS of ganitumab versus placebo in patients with higher levels of IGF-1, IGF-2, and IGFBP-3 was 16 versus 6.8 months (HR, 0.25; 95% CI: 0.09-0.67), 16 versus 5.9 months (HR, 0.24; 95% CI: 0.09-0.68), and 16 versus 6.8 months (HR, 0.28; 95% CI: 0.11-0.73), and in patients with lower IGFBP-2 levels was 12.7 versus 6.6 months (HR, 0.19; 95% CI: 0.07-0.55). Interaction between treatment and IGFs/IGFBPs in multivariate analyses suggested predictive potential for IGF-2 (P = 0.002) and IGFBP-2 (P = 0.02). KRAS mutation status and PTEN expression were not associated with OS. CONCLUSIONS: Baseline circulating factors of the IGF axis may predict OS benefit from ganitumab plus

gemcitabine in metastatic pancreatic adenocarcinoma. Clin Cancer Res; 19(15); 4282-9. ©2013 AACR.

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[13]

TÍTULO / TITLE: - Pancreatic tumor mass in a xenograft mouse model is decreased by treatment with therapeutic stem cells following introduction of therapeutic genes.

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

REVISTA / JOURNAL: - Oncol Rep. 2013 Jun 25. doi: 10.3892/or.2013.2564.

●● Enlace al texto completo (gratuito o de pago) 3892/or.2013.2564

AUTORES / AUTHORS: - Kim DJ; Yi BR; Lee HR; Kim SU; Choi KC

INSTITUCIÓN / INSTITUTION: - Laboratory of Veterinary Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University, Cheongju, Chungbuk, Republic of Korea.

RESUMEN / SUMMARY: - Pancreatic cancer is the fourth most common cause of cancer-related mortality. In the present study, we employed 2 types of therapeutic stem cells expressing cytosine deaminase (CD) with or without human interferon-beta (IFNbeta), HB1.F3.CD and HB1.F3.CD.IFN-beta cells, respectively, to selectively treat pancreatic cancer. The CD gene converts the non-toxic prodrug, 5-flurorocytosine (5-FC), into the toxic agent, 5-fluorouracil (5-FU). In addition, human IFN-beta is a potent cytokine that has antitumor effects. To generate a xenograft mouse model, PANC-1 cells (2x106/mouse) cultured in DMEM containing 10% FBS were mixed with Matrigel and were subcutaneously injected into Balb/c nu/nu mice. In the migration assay, the stem cells expressing the CD or IFN-beta gene effectively migrated toward the pancreatic cancer cells, suggesting the presence of chemoattractant factors secreted by the pancreatic tumors. In the co-culture and MTT assay, antitumor activity of the therapeutic stem cells was observed in the presence of 5-FC was shown that the growth of PANC-1 cells was inhibited. Furthermore, these effects were confirmed in the xenograft mouse model bearing tumors originating from PANC-1 cells. Analyses by histological and fluorescence microscopy showed that treatment with the stem cells resulted in the inhibition of pancreatic cancer growth in the presence of 5-FC. Taken together, these results indicate that stem cells expressing the CD and/or IFN-beta gene can be used to effectively treat pancreatic cancer and reduce the side-effects associated with conventional therapies.

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[14]

TÍTULO / TITLE: - Isolation and in vitro culture of rare cancer stem cells from patient-derived xenografts of pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Anal Chem. 2013 Aug 6;85(15):7271-8. doi: 10.1021/ac401165s. Epub 2013 Jul 15.

●● Enlace al texto completo (gratuito o de pago) 1021/ac401165s

AUTORES / AUTHORS: - Gach PC; Attayek PJ; Herrera G; Yeh JJ; Allbritton NL

INSTITUCIÓN / INSTITUTION: - Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27599, United States.

RESUMEN / SUMMARY: - Described is the construction of a large array of releasable microstructures (micropallets) along with screening and isolation protocols for sorting rare, approximately 1 in 10 000, cancer stem cells (CSCs) from a heterogeneous cell population. A 10.1 x 7.1 cm array of micropallets (50 x 50 x 75 mum structures and 25 mum micropallet gap) was fabricated on a large glass substrate, providing an array of approximately 1.3 million releasable microstructures. Image analysis algorithms were developed to permit array screening for identification of fluorescently labeled cells in less than 15 min using an epifluorescent wide-field microscope with a computer controlled translational stage. Device operation was tested by culturing HeLa cells transfected with green fluorescent protein (GFP) admixed with wild-type HeLa cells at ratios of 1:10(4) to 1:10(6) on the array followed by screening to identify flourescent cells. Micropallets containing cells of interest were then selectively released by a focused laser pulse and collected on a numbered poly(dimethylsiloxane) (PDMS) substrate with high viability. A direct comparison of this technology with fluorescence-activated cell sorting (FACS) demonstrated that micropallet arrays offered enhanced post sorting purity (100%), yield (100%), and viability (94-100%) for rare cell isolation. As a demonstration of the technology's value, pancreatic tumor cells from Panc-1 cell lines and patient-derived xenografts were screened for the presence of CD24, CD44, and CD326: surface markers of pancreatic CSCs. Following cell isolation and culture, 63 +/- 23% of the isolated Panc-1 cells and 35% of sorted human xenograft cells formed tumor spheroids retaining high expression levels of CD24, CD44, and CD326. The ability to isolate rare cells from relatively small sample sizes will facilitate our understanding of cell biology and the development of new therapeutic strategies.

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[15]

TÍTULO / TITLE: - Activated Pancreatic Stellate Cells Sequester CD8+ T-Cells to Reduce Their Infiltration of the Juxtatumoral Compartment of Pancreatic Ductal Adenocarcinoma.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Jul 25. pii: S0016-5085(13)01076-7. doi: 10.1053/j.gastro.2013.07.025.

●● Enlace al texto completo (gratuito o de pago) 1053/j.gastro.2013.07.025

AUTORES / AUTHORS: - Ene-Obong A; Clear AJ; Watt J; Wang J; Fatah R; Riches JC; Marshall JF; Chin-Aleong J; Chelala C; Gribben JG; Ramsay AG; Kocher HM

INSTITUCIÓN / INSTITUTION: - Centre for Tumour Biology, Queen Mary University of London, London EC1M 6BQ, UK.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Pancreatic ductal adenocarcinoma (PDAC) is characterized by a prominent desmoplastic microenvironment that contains many different immune cells. Activated pancreatic stellate cells (PSCs) contribute to the desmoplasia. We investigated whether distinct stromal compartments are differentially infiltrated by different types of immune cells. METHOD: We used tissue microarray analysis to compare immune cell infiltration of different pancreatico-biliary diseased tissues (PDAC, ampullary carcinoma, cholangiocarcinoma, mucinous cystic neoplasm, chronic inflammation, and chronic pancreatitis), and juxtatumoral stromal (<100 mum from tumor) and panstromal compartments. We investigated the association between immune infiltrate and patient survival times. We analyzed T-cell migration and tumor infiltration in LSL-KrasG12D/+; LSL-Trp53R172H/+; Pdx-1-Cre (KPC) mice, and the effects of all-trans retinoic acid (ATRA) on these processes. RESULTS: Juxtatumoral compartments in PDAC samples from 2 independent groups of patients contained increased numbers of myeloperoxidase+ and CD68+ cells, compared with panstromal compartments. However, juxtatumoral compartments of PDACs contained fewer CD8+, FoxP3+, CD56+, or CD20+ cells than panstromal compartments, a distinction absent in ampullary carcinomas and cholangiocarcinomas. Patients with PDACs that had high densities of CD8+ T-cells in the juxtatumoral compartment had longer survival times than patients with lower densities. In KPC mice, administration of ATRA, which renders PSCs quiescent, increased numbers of CD8+ T-cells in juxtatumoral compartments. We found that activated PSCs express cytokines, chemokines, and adhesion molecules that regulate T-cell migration. In vitro migration assays showed that CD8+ T-cells from PDAC patients had increased chemotaxis towards activated PSCs, which secrete CXCL12, compared with quiescent PSC or tumor cells. These effects could be reversed by knockdown of CXCL12 or treatment of PSCs with ATRA. CONCLUSION: Based on studies of human PDAC samples and KPC mice, activated PSCs appear to reduce migration of CD8+ T-cells to juxtatumoral stromal compartments, preventing their access to cancer cells. Deregulated signaling by activated PSCs could prevent an effective anti-tumor immune response.

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[16]

TÍTULO / TITLE: - Hyperglycemia, Insulin Resistance, Impaired Pancreatic beta-Cell Function, and Risk of Pancreatic Cancer.

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

REVISTA / JOURNAL: - J Natl Cancer Inst. 2013 Jul 17;105(14):1027-1035. Epub 2013 Jul 11.

●● Enlace al texto completo (gratuito o de pago) 1093/jnci/djt123

AUTORES / AUTHORS: - Wolpin BM; Bao Y; Qian ZR; Wu C; Kraft P; Ogino S; Stampfer MJ; Sato K; Ma J; Buring JE; Sesso HD; Lee IM; Gaziano JM; McTiernan A; Phillips LS; Cochrane BB; Pollak MN; Manson JE; Giovannucci EL; Fuchs CS

INSTITUCIÓN / INSTITUTION: - Affiliations of authors: Department of Medicine, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA (BMW); Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA (BMW, ZRQ, SO, KS, CSF); Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA (YB, SO, MJS, JM, JEM, ELG, CSF); Department of Epidemiology, (CW, PK, MJS, JM, HDS, I-ML, JEM, ELG), Department of Biostatistics (PK), and Department of Nutrition (MJS, ELG), Harvard School of Public Health, Boston, MA; Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA (JEB, HDS, I-ML, JMG, JEM); Department of Ambulatory Care and Prevention, Harvard Medical School, Boston, MA (JEB); Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), VA Boston Healthcare System (JMG); Cancer Prevention Research Unit, Department of Oncology, Faculty of Medicine, McGill University, Montreal, Quebec, Canada (MNP); Fred Hutchinson Cancer Research Center, Seattle, WA (AM); Division of Endocrinology and Metabolism, Emory University School of Medicine, Atlanta, GA (LSP); University of Washington School of Nursing, Seattle, WA (BBC).

RESUMEN / SUMMARY: - BACKGROUND: Obesity and diabetes mellitus are associated with an increased risk of pancreatic cancer. These associations may be secondary to consequences of peripheral insulin resistance, pancreatic beta-cell dysfunction, or hyperglycemia itself. Hemoglobin A1c (HbA1c) is a measure of hyperglycemia, whereas plasma insulin and proinsulin are markers of peripheral insulin resistance, and the proinsulin to insulin ratio marks pancreatic beta-cell dysfunction. METHODS: This was a prospective, nested case-control study of 449 case patients and 982 control subjects with prediagnostic blood samples and no diabetes history from five prospective US cohorts followed through 2008. Two or three control subjects were matched to each case patient by year of birth, cohort, smoking, and fasting status. Pancreatic cancer risk was assessed by prediagnostic HbA1c, insulin, proinsulin, and proinsulin to insulin ratio with multivariable-adjusted logistic regression. All P values were two-sided. RESULTS: The highest vs lowest quintiles of HbA1c, insulin, and proinsulin were associated with with an increased risk for pancreatic cancer (odds ratio [OR] = 1.79; 95% confidence interval [CI] = 1.17 to 2.72, P trend = .04 for HbA1c; OR = 1.57; 95% CI = 1.08 to 2.30; Ptrend = .002 for insulin; and OR = 2.22; 95% CI = 1.50 to 3.29; P trend < .001 for proinsulin). Proinsulin to

insulin ratio was not associated with pancreatic cancer risk. Results were similar across studies (all P heterogeneity > .29). In cancers developing 10 or more years after blood collection, the associations with insulin and proinsulin became stronger (highest vs lowest quintile, OR = 2.77; 95% CI = 1.28 to 5.99 for insulin and OR = 3.60; 95% CI = 1.68 to 7.72 for proinsulin). In mutually adjusted models including HbA1c, insulin, and proinsulin, only proinsulin remained statistically significant (highest vs lowest quintile, OR = 2.55; 95% CI = 1.54 to 4.21; Ptrend < .001). CONCLUSIONS: Among participants from five large prospective cohorts, circulating markers of peripheral insulin resistance, rather than hyperglycemia or pancreatic beta-cell dysfunction, were independently associated with pancreatic cancer risk.

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[17]

TÍTULO / TITLE: - A Gene Expression Signature of Epithelial Tubulogenesis and a Role for ASPM in Pancreatic Tumor Progression.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Jul 26. pii: S0016-5085(13)01122-0. doi: 10.1053/j.gastro.2013.07.040.

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

1053/j.gastro.2013.07.040

AUTORES / AUTHORS: - Wang WY; Hsu CC; Wang TY; Li CR; Hou YC; Chu JM; Lee CT; Liu MS; Su JJ; Jian KY; Huang SS; Jiang SS; Shan YS; Lin PW; Shen YY; Lee MT; Chan TS; Chang CC; Chen CH; Chang IS; Lee YL; Chen LT; Tsai KK

INSTITUCIÓN / INSTITUTION: - National Institute of Cancer Research and Translational Center for Glandular Malignancies, National Health Research Institutes, Tainan, 70456, Taiwan; Departments of Medicine, ,, Tainan, 70403, Taiwan.

RESUMEN / SUMMARY: - BACKGROUND: & Aims: Many patients with pancreatic ductal adenocarcinoma (PDAC) develop recurrent or metastatic diseases following surgery, so it is important to identify those most likely to benefit from aggressive therapy. Disruption of tissue microarchitecture is an early step in pancreatic tumorigenesis and a parameter used in pathology grading of glandular tumors. We investigated whether changes in gene expression during pancreatic epithelial morphogenesis were associated with outcomes of patients with PDAC after surgery. METHODS: We generated architectures of human pancreatic duct epithelial (HPDE) cells in a 3-dimensional basement membrane matrix. We identified gene expression profiles of the cells during different stages of tubular morphogenesis (tubulogenesis) and of PANC-1 cells during spheroid formation. Differential expression of genes was confirmed by immunoblot analysis. We compared the gene expression profile associated with pancreatic epithelial tubulogenesis with that of PDAC samples from 27 patients, as well as with their outcomes after surgery. RESULTS: We identified a gene expression

profile associated with tubulogenesis that resembled the profile of human pancreatic tissue with differentiated morphology and exocrine function. Patients with PDACs with this profile fared well following surgery. Based on this profile, we established a 6-28 gene tubulogenesis-specific signature that accurately determined the prognosis of independent cohorts of patients with PDAC (total n = 128; accuracy = 81.2%-95.0%). One gene ASPM, was downregulated during tubulogenesis, but upregulated in human PDAC cell lines and tumor samples; upregulation correlated with patient outcome (Cox regression P = .0028). Bioinformatic, genetic, biochemical, functional, and clinical correlative studies showed that ASPM promotes aggressiveness of PDAC by maintaining Wnt-beta-catenin signaling and stem cell features of PDAC cells. CONCLUSIONS: We identified a gene expression profile associated with pancreatic epithelial tubulogenesis and a tissue architecture-specific signature of PDAC cells that is associated with patient outcome following surgery.

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[18]

TÍTULO / TITLE: - Neoadjuvant Chemotherapy with Gemcitabine and S-1 for Resectable and Borderline Pancreatic Ductal Adenocarcinoma: Results from a Prospective Multi-institutional Phase 2 Trial.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Jul 10.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3129-9

AUTORES / AUTHORS: - Motoi F; Ishida K; Fujishima F; Ottomo S; Oikawa M; Okada T; Shimamura H; Takemura S; Ono F; Akada M; Nakagawa K; Katayose Y; Egawa S; Unno M

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterological Surgery, Department of Surgery, Graduate School of Medicine, Tohoku University, Sendai, Japan, fmotoi@surg1.med.tohoku.ac.jp.

RESUMEN / SUMMARY: - BACKGROUND: Surgical resection is the only curative strategy for pancreatic ductal adenocarcinoma (PDAC), but recurrence rates are high even after purported curative resection. First-line treatment with gemcitabine and S-1 (GS) is associated with promising antitumor activity with a high response rate. The aim of this study was to assess the feasibility and efficacy of GS in the neoadjuvant setting. METHODS: In a multi-institutional single-arm phase 2 study, neoadjuvant chemotherapy (NAC) with gemcitabine and S-1, repeated every 21 days, was administered for two cycles (NAC-GS) to patients with resectable and borderline PDAC. The primary end point was the 2-year survival rate. Secondary end points were feasibility, resection rate, pathological effect, recurrence-free survival, and tumor marker status. RESULTS: Of 36 patients enrolled, 35 were eligible for this clinical trial conducted between 2008 and 2010. The most common toxicity was neutropenia in response to 90 % of the relative dose intensity. Responses to NAC included

radiological tumor shrinkage (69 %) and decreases in CA19-9 levels (89 %). R0 resection was performed for 87 % in resection, and the morbidity rate (40 %) was acceptable. The 2-year survival rate of the total cohort was 45.7 %. Patients who underwent resection without metastases after NAC-GS (n = 27) had an increased median overall survival (34.7 months) compared with those who did not undergo resection (P = 0.0017). CONCLUSIONS: NAC-GS was well tolerated and safe when used in a multi-institutional setting. The R0 resection rate and the 2-year survival rate analysis are encouraging for patients with resectable and borderline PDAC.

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[19]

TÍTULO / TITLE: - Dietary fat intake and risk of pancreatic cancer in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial.

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

REVISTA / JOURNAL: - Ann Epidemiol. 2013 Jul 23. pii: S1047-2797(13)00169-5. doi: 10.1016/j.annepidem.2013.06.006.

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

1016/j.annepidem.2013.06.006

AUTORES / AUTHORS: - Arem H; Mayne ST; Sampson J; Risch H; Stolzenberg-Solomon RZ

INSTITUCIÓN / INSTITUTION: - Department of Chronic Disease Epidemiology, Yale University School of Public Health, New Haven, CT; Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD. Electronic address: aremhe2@mail.nih.gov.

RESUMEN / SUMMARY: - PURPOSE: Epidemiologic and experimental studies suggest that dietary fat intake may affect risk of pancreatic cancer, but published results are inconsistent. METHODS: We examined risk associations for specific types of dietary fat intakes and related food sources among 111,416 participants in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. We used Cox proportional hazards regression to examine associations between fat intake and pancreatic cancer risk. RESULTS: Over a mean 8.4 years of follow-up, 411 pancreatic cancer cases were identified. We observed an inverse association between saturated fat intake and pancreatic cancer risk (hazard ratio [HR], 0.64 comparing extreme quintiles; 95% confidence interval [CI], 0.46-0.88), but the association became weaker and nonsignificant when individuals with fewer than 4 years of follow-up were excluded to avoid possible reverse causation (HR, 0.88; 95% CI, 0.58-1.33). Total fat intake showed a similar pattern of association, whereas intakes of monounsaturated and polyunsaturated fats and fats from animal or plant sources showed no associations with risk. CONCLUSIONS: These results do not support the hypothesis of increased pancreatic cancer risk with higher fat consumption overall or by specific fat type or source. Dietary changes owing to

undetected disease may explain the observed inverse association with saturated fat.

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[20]

TÍTULO / TITLE: - Numb regulates acinar cell dedifferentiation and survival during pancreatic damage and acinar to ductal metaplasia.

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

REVISTA / JOURNAL: - Gastroenterology. 2013 Jul 24. pii: S0016-5085(13)01078-0. doi: 10.1053/j.gastro.2013.07.027.

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

1053/j.gastro.2013.07.027

AUTORES / AUTHORS: - Greer RL; Staley BK; Liou A; Hebrok M

INSTITUCIÓN / INSTITUTION: - Diabetes Center, Department of Medicine, University of California, San Francisco, San Francisco, CA, USA.

RESUMEN / SUMMARY: - BACKGROUND: & Aims: Pancreatic ductal adenocarcinoma (PDA) is a leading cause of cancer-related death. Through the process of acinar to ductal metaplasia (ADM), pancreatic acinar cells give rise to pancreatic intraepithelial neoplasia (PanIN), the most common precursor of PDA. However, even when Kras is activated in a majority of acinar cells, ADM and subsequent development of PanINs is inefficient in the absence of additional stresses. Numb regulates cell junctions, integrins and the activity of embryonic signaling pathways, therefore we investigated its effects on acinar cell dedifferentiation, regeneration and metaplasia. METHODS: We used mouse models of pancreatic regeneration and PDA, and also mice with loss-of-function alleles of Numb (p48Cre/p48CreER;Numbf/f and p48Cre/p48CreER;KrasG12D;Numbf/f mice) to study the roles of Numb in pancreatic regeneration and ADM. RESULTS: Loss of Numb resulted in premature dedifferentiation of acinar cells in response to injury due to administration of the cholecystokinin analog caerulein, and interfered with acinar cell regeneration. Numb was found to regulate multiple signaling pathways in acinar cells during caerulein-induced pancreatitis. Disruption of Numb accelerated and destabilized ADM in the context of oncogenic Kras (in p48Cre;KrasG12D;Numbf/f and p48CreER;KrasG12D;Numbf/f mice). CONCLUSIONS: Numb is an important regulator of acinar cell differentiation and viability during metaplasia. In mice with pancreatitis or pancreatic injury, elimination of Numb causes dedifferentiated acinar cells to undergo apoptosis-a process that is not mitigated by oncogenic Kras.

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[21]

TÍTULO / TITLE: - Circulating nucleosomes and immunogenic cell death markers HMGB1, sRAGE and DNAse in patients with advanced pancreatic cancer undergoing chemotherapy.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Int J Cancer. 2013 Jun 1. doi: 10.1002/ijc.28294.
●● Enlace al texto completo (gratuito o de pago) 1002/ijc.28294
AUTORES / AUTHORS: - Wittwer C; Boeck S; Heinemann V; Haas M; Stieber P; Nagel D; Holdenrieder S
INSTITUCIÓN / INSTITUTION: - Institute of Clinical Chemistry, University Hospital Munich-Grosshadern, Munich, Germany.
RESUMEN / SUMMARY: - Serum biomarkers are urgently needed for patient stratification and efficient treatment monitoring in pancreatic cancer (PC). Within a prospective diagnostic observation study, blood samples were obtained from 78 patients with advanced PC before and weekly during the course of palliative chemotherapy. Circulating nucleosomes and immunogenic cell death markers, high-mobility group box 1 (HMGB1), soluble receptors of advanced glycation end products (sRAGE) and DNAse activity, were measured by enzyme-linked immunosorbent assay and correlated with results of radiological staging after 2 months of treatment, with time to progression (TTP) and overall survival (OS). Median TTP and OS of PC patients were 3.9 and 7.7 months, respectively. Pretherapeutic baseline biomarker levels did not correlate with objective response; however, nucleosome levels on day (d) 28 were higher ($p = 0.048$) and sRAGE levels at time of staging (d56) were lower in progressive patients ($p = 0.046$). Concerning estimation of prognosis, high nucleosome levels (d7, d14, d21 and d56), low sRAGE levels (d56) and DNAse activity courses (d0-d7) correlated with TTP, whereas high nucleosomes (d7, d14 and d56), high HMGB1 (d21 and d56) and DNAse (d0-d7) were associated with OS. After adjustment to Karnofsky performance score, nucleosomes and HMGB1 (both d56) and DNAse (d0-d7) remained independent prognostic factors. Thus, courses of circulating nucleosomes and immunogenic cell death markers HMGB1 and sRAGE show prognostic relevance in PC patients undergoing chemotherapy.

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[22]
TÍTULO / TITLE: - Current understanding of the molecular biology of pancreatic neuroendocrine tumors.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Natl Cancer Inst. 2013 Jul 17;105(14):1005-17. doi: 10.1093/jnci/djt135. Epub 2013 Jul 9.
●● Enlace al texto completo (gratuito o de pago) 1093/jnci/djt135
AUTORES / AUTHORS: - Zhang J; Francois R; Iyer R; Seshadri M; Zajac-Kaye M; Hochwald SN
INSTITUCIÓN / INSTITUTION: - Affiliations of authors: Department of Surgical Oncology (JZ, SNH), Department of Medical Oncology (RI), and Department of Pharmacology and Therapeutics (MS), Roswell Park Cancer Institute, Buffalo,

NY; Department of Anatomy and Cell Biology, University of Florida College of Medicine, Gainesville, FL (RF, MZ-K).

RESUMEN / SUMMARY: - Pancreatic neuroendocrine tumors (PanNETs) are complicated and often deadly neoplasms. A recent increased understanding of their molecular biology has contributed to expanded treatment options. DNA sequencing of samples derived from patients with PanNETs and rare genetic syndromes such as multiple endocrine neoplasia type 1 (MEN1) and Von Hippel-Lindau (VHL) syndrome reveals the involvement of MEN1, DAXX/ATRX, and the mammalian target of rapamycin (mTOR) pathways in PanNET tumorigenesis. Gene knock-out/knock-in studies indicate that inactivation of factors including MEN1 and abnormal PI3K/mTOR signaling uncouples endocrine cell cycle progression from the control of environmental cues such as glucose, leading to islet cell overgrowth. In addition, accumulating evidence suggests that further impairment of endothelial-endocrine cell interactions contributes to tumor invasion and metastasis. Recent phase III clinical trials have shown that therapeutic interventions, such as sunitinib and everolimus, targeting those signal transduction pathways improve disease-free survival rates. Yet, cure in the setting of advanced disease remains elusive. Further advances in our understanding of the molecular mechanisms of PanNETs and improved preclinical models will assist in developing personalized therapy utilizing novel drugs to provide prolonged control or even cure the disease.

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[23]

TÍTULO / TITLE: - Total pancreatectomy with islet autotransplantation in patients with malignancy: are we there yet?

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

REVISTA / JOURNAL: - Ann Surg. 2013 Aug;258(2):219-20. doi: 10.1097/SLA.0b013e31829c4a1b.

●● Enlace al texto completo (gratuito o de pago) 1097/SLA.0b013e31829c4a1b

AUTORES / AUTHORS: - Dudeja V; Beilman GJ; Vickers SM

INSTITUCIÓN / INSTITUTION: - From the Department of Surgery, University of Minnesota, Minneapolis, MN.

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[24]

TÍTULO / TITLE: - Inactivating mutations of RNF43 confer Wnt dependency in pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Jul 30;110(31):12649-54. doi: 10.1073/pnas.1307218110. Epub 2013 Jul 11.

●● Enlace al texto completo (gratuito o de pago) 1073/pnas.1307218110

AUTORES / AUTHORS: - Jiang X; Hao HX; Growney JD; Woolfenden S; Bottiglio C; Ng N; Lu B; Hsieh MH; Bagdasarian L; Meyer R; Smith TR; Avello M; Charlat O; Xie Y; Porter JA; Pan S; Liu J; McLaughlin ME; Cong F

INSTITUCIÓN / INSTITUTION: - Developmental and Molecular Pathways, Novartis Institutes for Biomedical Research, Cambridge, MA 02139.

RESUMEN / SUMMARY: - A growing number of agents targeting ligand-induced Wnt/beta-catenin signaling are being developed for cancer therapy. However, clinical development of these molecules is challenging because of the lack of a genetic strategy to identify human tumors dependent on ligand-induced Wnt/beta-catenin signaling. Ubiquitin E3 ligase ring finger 43 (RNF43) has been suggested as a negative regulator of Wnt signaling, and mutations of RNF43 have been identified in various tumors, including cystic pancreatic tumors. However, loss of function study of RNF43 in cell culture has not been conducted, and the functional significance of RNF43 mutations in cancer is unknown. Here, we show that RNF43 inhibits Wnt/beta-catenin signaling by reducing the membrane level of Frizzled in pancreatic cancer cells, serving as a negative feedback mechanism. Inhibition of endogenous Wnt/beta-catenin signaling increased the cell surface level of Frizzled. A panel of 39 pancreatic cancer cell lines was tested for Wnt dependency using LGK974, a selective Porcupine inhibitor being examined in a phase 1 clinical trial. Strikingly, all LGK974-sensitive lines carried inactivating mutations of RNF43. Inhibition of Wnt secretion, depletion of beta-catenin, or expression of wild-type RNF43 blocked proliferation of RNF43 mutant but not RNF43-wild-type pancreatic cancer cells. LGK974 inhibited proliferation and induced differentiation of RNF43-mutant pancreatic adenocarcinoma xenograft models. Our data suggest that mutational inactivation of RNF43 in pancreatic adenocarcinoma confers Wnt dependency, and the presence of RNF43 mutations could be used as a predictive biomarker for patient selection supporting the clinical development of Wnt inhibitors in subtypes of cancer.

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[25]

- CASTELLANO -

TÍTULO / TITLE: Intensitatsmodulierte Radiotherapie als neoadjuvante Radiochemotherapie zur Behandlung von Patienten mit lokal fortgeschrittenem Pankreaskarzinom : Ergebnisanalyse und Vergleich mit einer Patientenkohorte mit 3-D-Strahlentherapie.

TÍTULO / TITLE: - Intensity modulated radiotherapy as neoadjuvant chemoradiation for the treatment of patients with locally advanced pancreatic cancer : Outcome analysis and comparison with a 3D-treated patient cohort.

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

REVISTA / JOURNAL: - Strahlenther Onkol. 2013 Jul 31.

●● Enlace al texto completo (gratuito o de pago) 1007/s00066-013-0391-5

AUTORES / AUTHORS: - Combs SE; Habermehl D; Kessel K; Bergmann F; Werner J; Brecht I; Schirmacher P; Jager D; Buchler MW; Debus J

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University Hospital of Heidelberg, Im Neuenheimer Feld 400, 69120, Heidelberg, Germany, Stephanie.Combs@med.uni-heidelberg.de.

RESUMEN / SUMMARY: - BACKGROUND: To evaluate outcome after intensity modulated radiotherapy (IMRT) compared to 3D conformal radiotherapy (3D-RT) as neoadjuvant treatment in patients with locally advanced pancreatic cancer (LAPC). MATERIALS AND METHODS: In total, 57 patients with LAPC were treated with IMRT and chemotherapy. A median total dose of 45 Gy to the PTV_baseplan and 54 Gy to the PTV_boost in single doses of 1.8 Gy for the PTV_baseplan and median single doses of 2.2 Gy in the PTV_boost were applied. Outcomes were evaluated and compared to a large cohort of patients treated with 3D-RT. RESULTS: Overall treatment was well tolerated in all patients and IMRT could be completed without interruptions. Median overall survival was 11 months (range 5-37.5 months). Actuarial overall survival at 12 and 24 months was 36 % and 8 %, respectively. A significant impact on overall survival could only be observed for a decrease in CA 19-9 during treatment, patients with less pre-treatment CA 19-9 than the median, as well as weight loss during treatment. Local progression-free survival was 79 % after 6 months, 39 % after 12 months, and 13 % after 24 months. No factors significantly influencing local progression-free survival could be identified. There was no difference in overall and progression-free survival between 3D-RT and IMRT. Secondary resectability was similar in both groups (26 % vs. 28 %). Toxicity was comparable and consisted mainly of hematological toxicity due to chemotherapy. CONCLUSION: IMRT leads to a comparable outcome compared to 3D-RT in patients with LAPC. In the future, the improved dose distribution, as well as advances in image-guided radiotherapy (IGRT) techniques, may improve the use of IMRT in local dose escalation strategies to potentially improve outcome.

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[26]

TÍTULO / TITLE: - Increased neutrophil-lymphocyte ratio is a poor prognostic factor in patients with primary operable and inoperable pancreatic cancer.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Jul 23;109(2):416-21. doi: 10.1038/bjc.2013.332. Epub 2013 Jun 25.

●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.332

AUTORES / AUTHORS: - Stotz M; Gerger A; Eisner F; Szkandera J; Loibner H; L Ress A; Kornprat P; A Zoughbi W; Seggewies FS; Lackner C; Stojakovic T; Samonigg H; Hoefler G; Pichler M

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

RESUMEN / SUMMARY: - Background:The neutrophil-lymphocyte ratio (NLR) has been proposed as an indicator of systemic inflammatory response. Previous findings from small-scale studies revealed conflicting results about its independent prognostic significance with regard to different clinical end points in pancreatic cancer (PC) patients. Therefore, the aim of our study was the external validation of the prognostic significance of NLR in a large cohort of PC patients.Methods:Data from 371 consecutive PC patients, treated between 2004 and 2010 at a single centre, were evaluated retrospectively. The whole cohort was stratified into two groups according to the treatment modality. Group 1 comprised 261 patients with inoperable PC at diagnosis and group 2 comprised 110 patients with surgically resected PC. Cancer-specific survival (CSS) was assessed using the Kaplan-Meier method. To evaluate the independent prognostic significance of the NLR, the modified Glasgow prognostic score (mGPS) and the platelet-lymphocyte ratio univariate and multivariate Cox regression models were applied.Results:Multivariate analysis identified increased NLR as an independent prognostic factor for inoperable PC patients (hazard ratio (HR)=2.53, confidence interval (CI)=1.64-3.91, P<0.001) and surgically resected PC patients (HR=1.61, CI=1.02-2.53, P=0.039). In inoperable PC patients, the mGPS was associated with poor CSS only in univariate analysis (HR=1.44, CI=1.04-1.98).Conclusion:Risk prediction for cancer-related end points using NLR does add independent prognostic information to other well-established prognostic factors in patients with PC, regardless of the undergoing therapeutic modality. Thus, the NLR should be considered for future individual risk assessment in patients with PC.

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[27]

TÍTULO / TITLE: - Pulmonary embolism diagnosed with EUS on a patient with adenocarcinoma of the pancreas (with video).

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

REVISTA / JOURNAL: - Gastrointest Endosc. 2013 Jun 12. pii: S0016-5107(13)01868-3. doi: 10.1016/j.gie.2013.05.001.

●● Enlace al texto completo (gratuito o de pago) 1016/j.gie.2013.05.001

AUTORES / AUTHORS: - Tee CT; Chen HC; Segarajasingam DS; Yusoff IF

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Sir Charles Gairdner Hospital, Perth, Australia.

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[28]

TÍTULO / TITLE: - NADPH oxidase activation in pancreatic cancer cells is mediated through Akt-dependent up-regulation of p22phox.

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

REVISTA / JOURNAL: - J Biol Chem. 2013 Jul 5;288(27):19648. doi: 10.1074/jbc.A110.200063.

●● Enlace al texto completo (gratuito o de pago) 1074/jbc.A110.200063

AUTORES / AUTHORS: - Edderkaoui M; Nitsche C; Zheng L; Pandol SJ; Gukovsky I; Gukovskaya AS

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[29]

TÍTULO / TITLE: - Silencing of decoy receptor 3 (DcR3) expression by siRNA in pancreatic carcinoma cells induces Fas ligand-mediated apoptosis in vitro and in vivo.

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

REVISTA / JOURNAL: - Int J Mol Med. 2013 Sep;32(3):653-60. doi: 10.3892/ijmm.2013.1437. Epub 2013 Jul 11.

●● Enlace al texto completo (gratuito o de pago) 3892/ijmm.2013.1437

AUTORES / AUTHORS: - Zhou J; Song S; He S; Wang Z; Zhang B; Li D; Zhu D

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu 215006, P.R. China.

RESUMEN / SUMMARY: - Decoy receptor 3 (DcR3) is abundantly expressed in human tumors and protects cells from a wide range of apoptotic stimuli. In this study, we demonstrate that DcR3 is overexpressed in pancreatic carcinoma cells, and that the pancreatic carcinoma cell lines, Panc-1 and SW1990, are resistant to Fas ligand (FasL)-mediated apoptosis. To further define the function of DcR3 in cell growth and apoptosis, we used small interfering RNA (siRNA) to knockdown the expression of the DcR3 gene in Panc-1 and SW1990 cells. Our results revealed that the silencing of DcR3 expression enhanced the inhibitory effects of FasL and reduced the capabiltiy of the cells for proliferation and colony formation in vitro. In addition, the downregulation of DcR3 modulated the cell apoptotic regulators, Fas-associated death domain (FADD), caspase3 and caspase8, thus triggering cell apoptosis. Furthermore, the knockdown of DcR3 inhibited the growth of Panc-1 tumor xenografts. Taken together, our findings indicate that DcR3 is important in cancer progression and may be a used as a potential therapeutic target for the gene therapy of pancreatic carcinoma.

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[30]

TÍTULO / TITLE: - A prospective, phase ½ study of everolimus and temozolomide in patients with advanced pancreatic neuroendocrine tumor.

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

REVISTA / JOURNAL: - Cancer. 2013 Jun 3. doi: 10.1002/cncr.28142.

●● Enlace al texto completo (gratuito o de pago) 1002/cncr.28142

AUTORES / AUTHORS: - Chan JA; Blaszkowsky L; Stuart K; Zhu AX; Allen J; Wadlow R; Ryan DP; Meyerhardt J; Gonzalez M; Regan E; Zheng H; Kulke MH

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts; Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts; Harvard Medical School, Boston, Massachusetts.

RESUMEN / SUMMARY: - BACKGROUND: Both everolimus and temozolomide are associated with single-agent activity in patients with pancreatic neuroendocrine tumor (NET). A phase ½ study was performed to evaluate the safety and efficacy of temozolomide in combination with everolimus in patients who have advanced pancreatic NET. METHODS: Patients were treated with temozolomide at a dose of 150 mg/m2 per day on days 1 through 7 and days 15 through 21 in combination with everolimus daily in each 28-day cycle. In cohort 1, temozolomide was administered together with everolimus at 5 mg daily. Following demonstration of safety in this cohort, subsequent patients in cohort 2 were treated with temozolomide plus everolimus at 10 mg daily. The duration of temozolomide treatment was limited to 6 months. Patients were followed for toxicity, radiologic and biochemical response, and survival. RESULTS: A total of 43 patients were enrolled, including 7 in cohort 1 and 36 in cohort 2. Treatment was associated with known toxicities of each drug; no synergistic toxicities were observed. Among 40 evaluable patients, 16 (40%) experienced a partial response. The median progression-free survival duration was 15.4 months. Median overall survival was not reached. CONCLUSIONS: Temozolomide and everolimus can be safely administered together in patients with advanced pancreatic NET, and the combination is associated with encouraging antitumor activity. Future studies evaluating the efficacy of combination therapy compared to treatment with either agent alone are warranted. Cancer 2013. © 2013 American Cancer Society.

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[31]

TÍTULO / TITLE: - Phase 2 study of erlotinib combined with adjuvant chemoradiation and chemotherapy in patients with resectable pancreatic cancer.

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

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Jul 15;86(4):678-85. doi: 10.1016/j.ijrobp.2013.03.032.

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

1016/j.ijrobp.2013.03.032

AUTORES / AUTHORS: - Herman JM; Fan KY; Wild AT; Hacker-Prietz A; Wood LD; Blackford AL; Ellsworth S; Zheng L; Le DT; De Jesus-Acosta A; Hidalgo M; Donehower RC; Schulick RD; Edil BH; Choti MA; Hruban RH; Pawlik TM; Cameron JL; Laheru DA; Wolfgang CL

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology and Molecular Radiation Sciences, Sidney Kimmel Comprehensive Cancer Center, Johns

Hopkins School of Medicine, Baltimore, Maryland 21231, USA. jherma15@jhmi.edu

RESUMEN / SUMMARY: - PURPOSE: Long-term survival rates for patients with resected pancreatic ductal adenocarcinoma (PDAC) have stagnated at 20% for more than a decade, demonstrating the need to develop novel adjuvant therapies. Gemcitabine-erlotinib therapy has demonstrated a survival benefit for patients with metastatic PDAC. Here we report the first phase 2 study of erlotinib in combination with adjuvant chemoradiation and chemotherapy for resected PDAC. METHODS AND MATERIALS: Forty-eight patients with resected PDAC received adjuvant erlotinib (100 mg daily) and capecitabine (800 mg/m(2) twice daily Monday-Friday) concurrently with intensity modulated radiation therapy (IMRT), 50.4 Gy over 28 fractions followed by 4 cycles of gemcitabine (1000 mg/m(2) on days 1, 8, and 15 every 28 days) and erlotinib (100 mg daily). The primary endpoint was recurrence-free survival (RFS). RESULTS: The median follow-up time was 18.2 months (interquartile range, 13.8-27.1). Lymph nodes were positive in 85% of patients, and margins were positive in 17%. The median RFS was 15.6 months (95% confidence interval [CI], 13.4-17.9), and the median overall survival (OS) was 24.4 months (95% CI, 18.9-29.7). Multivariate analysis with adjustment for known prognostic factors showed that tumor diameter >3 cm was predictive for inferior RFS (hazard ratio, 4.01; P=.001) and OS (HR, 4.98; P=.02), and the development of dermatitis was associated with improved RFS (HR, 0.27; P=.009). During CRT and post-CRT chemotherapy, the rates of grade ¾ toxicity were 31%/2% and 35%/8%, respectively. CONCLUSION: Erlotinib can be safely administered with adjuvant IMRT-based CRT and chemotherapy. The efficacy of this regimen appears comparable to that of existing adjuvant regimens. Radiation Therapy Oncology Group 0848 will ultimately determine whether erlotinib produces a survival benefit in patients with resected pancreatic cancer.

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[32]

TÍTULO / TITLE: - A phase II study of a personalized peptide vaccination for chemotherapy-resistant advanced pancreatic cancer patients.

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

REVISTA / JOURNAL: - Oncol Rep. 2013 Jun 20. doi: 10.3892/or.2013.2556.

●● Enlace al texto completo (gratuito o de pago) 3892/or.2013.2556

AUTORES / AUTHORS: - Yutani S; Komatsu N; Yoshitomi M; Matsueda S; Yonemoto K; Mine T; Noguchi M; Ishihara Y; Yamada A; Itoh K; Sasada T

INSTITUCIÓN / INSTITUTION: - Department of Immunology and Immunotherapy, Kurume University School of Medicine, Kurume, Fukuoka 830-0011, Japan.

RESUMEN / SUMMARY: - Pancreatic cancer is one of the most aggressive cancers with a median survival time (MST) of <6 months in chemotherapy-resistant patients. Therefore, the development of novel treatment modalities is needed. In the present study, a phase II study of personalized peptide

vaccination (PPV) was conducted, in which vaccine antigens were selected and administered based on the pre-existing IgG responses to 31 different pooled peptides, for 41 chemotherapy-resistant advanced pancreatic cancer patients. No vaccine-related severe adverse events were observed. IgG responses specific to at least one of the vaccine peptides were augmented in 14 of 36 patients (39%) and in 18 of 19 patients (95%) tested after the 5th and 11th vaccination, respectively. MST from the first vaccination was 7.9 months with a 1-year survival rate of 26.8%. Higher serum amyloid A (SAA) and C-reactive protein (CRP) levels in pre-vaccination plasma were unfavorable factors for overall survival (OS). Due to the safety profile and the potential clinical efficacy, the conduction of additional clinical trials of PPV for chemotherapy-resistant advanced pancreatic cancer patients is warranted.

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[33]

TÍTULO / TITLE: - Modest Improvement in Overall Survival for Patients With Metastatic Pancreatic Cancer: A Trend Analysis Using the Surveillance, Epidemiology, and End Results Registry From 1988 to 2008.

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

REVISTA / JOURNAL: - Pancreas. 2013 Jul 16.

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

1097/MPA.0b013e318291fbc5

AUTORES / AUTHORS: - Worni M; Guller U; White RR; Castleberry AW; Pietrobon R; Cerny T; Gloor B; Koeberle D

INSTITUCIÓN / INSTITUTION: - From the *Department of Surgery, Duke University Medical Center, Durham, NC; daggerDepartment of Visceral Surgery and Medicine, University of Bern, Bern; and double daggerDepartment of Medical Oncology and Hematology, Cantonal Hospital St Gallen, Gallen, Switzerland.

RESUMEN / SUMMARY: - OBJECTIVES: Patients with pancreatic adenocarcinoma often present with distant metastatic disease. We aimed to assess whether improvements in survival of clinical trials translated to a population-based level. METHODS: The US Surveillance, Epidemiology, and End Results registry was queried. Adult patients with distant metastatic adenocarcinoma of the pancreas were included from 1988 to 2008. Overall survival was analyzed using Kaplan-Meier curves as well as multivariable-adjusted Cox proportional hazards models. RESULTS: In total, 32,452 patients were included. Mean age was 67.6 (SD: 11.7) years, and 15,341 (47.3%) were female. Median overall survival was 3 months (95% confidence interval [CI], 3-3 months), which increased from 2 (CI, 2-2) months in 1988 to 3 (CI, 3-4) months in 2008. After adjustment for multiple covariates, the hazard ratio (HR) decreased by 0.977 per year (CI, 0.975-0.980). In multivariable-adjusted survival analyses, tumor location in the pancreatic body/tail (HR, 1.10), male sex (HR, 1.09), increasing age (HR, 1.016), African American ethnicity (HR, 1.16), nonmarried civil status (HR, 1.18), and absence of radiotherapy (HR,

1.41) were associated with worse survival (P < 0.001 for all predictors). CONCLUSIONS: The improvement in overall survival over the past 2 decades among patients with metastatic pancreatic adenocarcinoma is modest and disappointing. More effective therapeutic strategies for advanced disease are desperately needed.

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[34]

TÍTULO / TITLE: - A multinational phase 2 study of nanoliposomal irinotecan sucrosofate (PEP02, MM-398) for patients with gemcitabine-refractory metastatic pancreatic cancer.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Jul 23. doi: 10.1038/bjc.2013.408.

●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.408

AUTORES / AUTHORS: - Ko AH; Tempero MA; Shan YS; Su WC; Lin YL; Dito E; Ong A; Wang YW; Yeh CG; Chen LT

INSTITUCIÓN / INSTITUTION: - Division of Hematology/Oncology, Comprehensive Cancer Center, University of California, San Francisco, 1600 Divisadero Street, San Francisco, CA 94115, USA.

RESUMEN / SUMMARY: - Background:PEP02, also known as MM-398, is a novel nanoliposomal irinotecan that has improved pharmacokinetics and tumour bio-distribution of the free drug. This phase 2 study evaluated PEP02 monotherapy as second-line treatment for pancreatic cancer.Methods:Patients who had metastatic pancreatic adenocarcinoma, Karnofsky performance status >/=70, and had progressed following gemcitabine-based therapy were eligible. Intravenous injection of PEP02 120 mg m-2 was given every 3 weeks. Simon 2-stage design was used. The primary objective was 3-month survival rate (OS3-month).Results:A total of 40 patients were enrolled. The most common severe adverse events included neutropenia, abdominal pain, asthenia, and diarrhoea. Three patients (7.5%) achieved an objective response, with an additional 17 (42.5%) demonstrating stable disease for a minimum of two cycles. Ten (31.3%) of 32 patients with an elevated baseline CA19-9 had a >50% biomarker decline. The study met its primary end point with an OS3-month of 75%, with median progression-free survival and overall survival of 2.4 and 5.2 months, respectively.Conclusion:PEP02 demonstrates moderate antitumour activity with a manageable side effect profile for metastatic, gemcitabine-refractory pancreatic cancer patients. Given the limited treatment options available to this patient population, a phase 3 trial of PEP02 (MM-398), referred to as NAPOLI-1, is currently underway.British Journal of Cancer advance online publication, 23 July 2013; doi:10.1038/bjc.2013.408 www.bjcancer.com.

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[35]

TÍTULO / TITLE: - Treatment of human pancreatic cancer using combined ultrasound, microbubbles, and gemcitabine: A clinical case study.

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

REVISTA / JOURNAL: - Med Phys. 2013 Jul;40(7):072902. doi: 10.1118/1.4808149.

●● Enlace al texto completo (gratuito o de pago) 1118/1.4808149

AUTORES / AUTHORS: - Kotopoulis S; Dimcevski G; Gilja OH; Hoem D; Postema M

INSTITUCIÓN / INSTITUTION: - National Centre for Ultrasound in Gastroenterology, Haukeland University Hospital, Bergen 5021, Norway and Department of Physics and Technology, University of Bergen, Bergen 5007, Norway.

RESUMEN / SUMMARY: - Purpose: The purpose of this study was to investigate the ability and efficacy of inducing sonoporation in a clinical setting, using commercially available technology, to increase the patients' quality of life and extend the low Eastern Cooperative Oncology Group performance grade; as a result increasing the overall survival in patients with pancreatic adenocarcinoma.Methods: Patients were treated using a customized configuration of a commercial clinical ultrasound scanner over a time period of 31.5 min following standard chemotherapy treatment with gemcitabine. SonoVue(®) ultrasound contrast agent was injected intravascularly during the treatment with the aim to induce sonoporation.Results: Using the authors' custom acoustic settings, the authors' patients were able to undergo an increased number of treatment cycles; from an average of 9 cycles, to an average of 16 cycles when comparing to a historical control group of 80 patients. In two out of five patients treated, the maximum tumor diameter was temporally decreased to 80 +/- 5% and permanently to 70 +/- 5% of their original size, while the other patients showed reduced growth. The authors also explain and characterize the settings and acoustic output obtained from a commercial clinical scanner used for combined ultrasound microbubble and chemotherapy treatment.Conclusions: It is possible to combine ultrasound, microbubbles, and chemotherapy in a clinical setting using commercially available clinical ultrasound scanners to increase the number of treatment cycles, prolonging the quality of life in patients with pancreatic adenocarcinoma compared to chemotherapy alone.

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[36]

TÍTULO / TITLE: - miR-210 regulates the interaction between pancreatic cancer cells and stellate cells.

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

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Aug 2;437(3):433-9. doi: 10.1016/j.bbrc.2013.06.097. Epub 2013 Jul 4.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bbrc.2013.06.097

AUTORES / AUTHORS: - Takikawa T; Masamune A; Hamada S; Nakano E; Yoshida N; Shimosegawa T

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology, Tohoku University Graduate School of Medicine, Sendai, Japan.

RESUMEN / SUMMARY: - There is accumulating evidence that pancreatic stellate cells (PSCs) promote the progression of pancreatic cancer. microRNAs (miRNAs) are small non-coding RNAs acting as negative regulators of gene expression at the post-transcriptional level. This study aimed to clarify the role of miRNAs in the interaction between PSCs and pancreatic cancer cells. Pancreatic cancer cells were mono-cultured or indirectly co-cultured with PSCs. miRNAs were prepared, and Agilent's miRNA microarray containing probes for 904 human miRNAs was used to identify differentially expressed miRNAs. miR-210 was identified as an upregulated miRNA by co-culture with PSCs. Conditioned media of PSCs activated ERK and Akt, but not hypoxia-inducible factor-1alpha pathway. PSCs-induced miR-210 upregulation was inhibited by inhibitors of ERK and PI3K/Akt pathways. Inhibition of miR-210 expression decreased migration, decreased the expression of vimentin and snai-1, and increased the membrane-associated expression of beta-catenin in Panc-1 cells co-cultured with PSCs. In conclusion, our results suggest a novel role of miR-210 in the interaction between PSCs and pancreatic cancer cells.

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[37]

TÍTULO / TITLE: - FOXL1, a Novel Candidate Tumor Suppressor, Inhibits Tumor Aggressiveness and Predicts Outcome in Human Pancreatic Cancer.

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

REVISTA / JOURNAL: - Cancer Res. 2013 Jun 27.

●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-13-0362

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

INSTITUCIÓN / INSTITUTION: - Laboratory of Human Carcinogenesis, NCI/NIH.

RESUMEN / SUMMARY: - The Forkhead Box L1 (FOXL1) transcription factor regulates epithelial proliferation and development of gastrointestinal tract, and has been implicated in gastrointestinal tumorigenesis in mouse models. However, the role of FOXL1 in pancreatic cancer development and progression remains to be elucidated. Here, we report that a higher expression of FOXL1 is significantly associated with better clinical outcome in human pancreatic ductal adenocarcinoma (PDAC). A lower FOXL1 expression is correlated with metastasis and advanced pathological stage of pancreatic cancer. Mechanistic analyses demonstrated that over-expression of FOXL1 induces apoptosis and inhibits proliferation and invasion in pancreatic cancer cells, whereas silencing of FOXL1 by siRNA inhibits apoptosis and enhances tumor cell growth and invasion. Furthermore, FOXL1 overexpression significantly suppressed the

growth of tumor xenografts in nude mice. FOXL1 promoted apoptosis partly through the induction of TNF-related apoptosis-inducing ligand (TRAIL) in pancreatic cancer cells. In addition, FOXL1 suppressed the transcription of zinc finger E-box-binding homeobox 1 (ZEB1), an activator of epithelial mesenchymal transition (EMT), and the negative regulation of ZEB1 contributed to the inhibitory effect of FOXL1 on tumor cell invasion. Taken together, our findings suggest that FOXL1 expression is a candidate predictor of clinical outcome in patients with resected PDAC and it plays an inhibitory role in pancreatic tumor progression.

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[38]

TÍTULO / TITLE: - Insulinoma-released exosomes activate autoreactive marginal zone-like B cells that expand endogenously in prediabetic NOD mice.

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

REVISTA / JOURNAL: - Eur J Immunol. 2013 Jul 2. doi: 10.1002/eji.201343376.

●● Enlace al texto completo (gratuito o de pago) 1002/eji.201343376

AUTORES / AUTHORS: - Bashratyan R; Sheng H; Regn D; Rahman MJ; Dai YD

INSTITUCIÓN / INSTITUTION: - Division of Immune Regulation, Torrey Pines Institute for Molecular Studies, San Diego, CA, USA.

RESUMEN / SUMMARY: - Exosomes (EXOs) are nano-sized secreted microvesicles that can function as potent endogenous carriers of adjuvant and antigens. To examine a possible role in autoimmunity for EXOs, we studied EXO-induced immune responses in nonobese diabetic (NOD) mice, an autoimmune-prone strain with tissue-specific targeting at insulin-secreting beta cells. EXOs released by insulinoma cells can activate various antigen-presenting cells to secrete several proinflammatory cytokines and chemokines. A subset of B cells responded to EXO stimulation in culture by proliferation, and expressed surface markers representing marginal zone B cells, which was independent of T helper cells. Importantly, splenic B cells from prediabetic NOD mice, but not diabetic-resistant mice, exhibited increased reactivity to EXOs, which was correlated with a high level of serum EXOs. We found that MyD88-mediated innate TLR signals were essential for the B-cell response; transgenic B cells expressing surface immunoglobulin specific for insulin reacted to EXO stimulation, and addition of a calcineurin inhibitor FK506 abrogated the EXO-induced B-cell response, suggesting that both innate and antigen-specific signals may be involved. Thus, EXOs may contribute to the development of autoimmunity and type 1 diabetes in NOD mice, partially via activating autoreactive marginal zone-like B cells.

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[39]

TÍTULO / TITLE: - Current trends in preoperative biliary stenting in patients with pancreatic cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Surgery. 2013 Aug;154(2):179-89. doi: 10.1016/j.surg.2013.03.016.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.03.016

AUTORES / AUTHORS: - Jinkins LJ; Parmar AD; Han Y; Duncan CB; Sheffield KM; Brown KM; Riall TS

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The University of Texas Medical Branch, Galveston, TX.

RESUMEN / SUMMARY: - BACKGROUND: Sufficient evidence suggests that preoperative biliary stenting is associated with increased complication rates after pancreaticoduodenectomy. METHODS: Surveillance, Epidemiology, and End Results (SEER) and linked Medicare claims data (1992-2007) were used to identify patients with pancreatic cancer who underwent pancreaticoduodenectomy. We evaluated trends in the use of preoperative biliary stenting, timing of physician visits relative to stenting, and time to surgical resection and symptoms in stented and unstented patients. RESULTS: Pancreaticoduodenectomy was performed in 2,573 patients, and 52.6% of patients underwent preoperative biliary stenting (N = 1,354). Of these, 75.3% underwent endoscopic stenting only, 18.9% received a percutaneous stent, and 5.8% underwent both procedures. The overall stenting rate increased from 29.6% of patients between 1992 and 1995 to 59.1% between 2004 and 2007 (P < .0001). Preoperative stenting was more common in patients with jaundice, cholangitis, pruritus, or coagulopathy (P < .05 for all). Of stented patients, 77.7% had had a stent placed prior to seeing a surgeon. Stenting prior to surgical consultation was associated with longer indwelling stent time compared to stenting after surgical consultation (37.3 vs 27.0 days, P < .0001). In addition, stented patients had longer times from surgeon visit to pancreatectomy than those who had not received stents (24.2 days vs 17.2 days, P < .0001). CONCLUSION: Use of preoperative biliary stenting doubled between 1992 and 2007 despite evidence that stenting is associated with increased perioperative infectious complications. The majority of stenting occurred prior to surgical consultation and is associated with significant delay in time to operation. Surgeons should be involved early in order to prevent unnecessary stenting and improve outcomes.

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[40]

TÍTULO / TITLE: - Intravital FLIM-FRET Imaging Reveals Dasatinib-Induced Spatial Control of Src in Pancreatic Cancer.

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

REVISTA / JOURNAL: - Cancer Res. 2013 Aug 1;73(15):4674-4686. Epub 2013 Jun 7.

●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-12-4545

AUTORES / AUTHORS: - Nobis M; McGhee EJ; Morton JP; Schwarz JP; Karim SA; Quinn J; Edward M; Campbell AD; McGarry LC; Evans TR; Brunton VG; Frame MC; Carragher NO; Wang Y; Sansom OJ; Timpson P; Anderson KI
INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: The Beatson Institute for Cancer Research, Glasgow; Section of Dermatology, School of Medicine, University of Glasgow, Glasgow; Edinburgh Cancer Research Centre, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, United Kingdom; Department of Bioengineering, University of Illinois, Urbana-Champaign, Urbana-Champaign, Illinois; and The Garvan Institute of Medical Research and The Kinghorn Cancer Centre, Sydney, New South Wales; St. Vincent's Clinical School, Faculty of Medicine, University of New South Wales, New South Wales, Australia.
RESUMEN / SUMMARY: - Cancer invasion and metastasis occur in a complex three-dimensional (3D) environment, with reciprocal feedback from the surrounding host tissue and vasculature-governing behavior. In this study, we used a novel intravital method that revealed spatiotemporal regulation of Src activity in response to the anti-invasive Src inhibitor dasatinib. A fluorescence lifetime imaging microscopy-fluorescence resonance energy transfer (FLIM-FRET) Src biosensor was used to monitor drug-targeting efficacy in a transgenic p53-mutant mouse model of pancreatic cancer. In contrast to conventional techniques, FLIM-FRET analysis allowed for accurate, time-dependent, live monitoring of drug efficacy and clearance in live tumors. In 3D organotypic cultures, we showed that a spatially distinct gradient of Src activity exists within invading tumor cells, governed by the depth of penetration into complex matrices. In parallel, this gradient was also found to exist within live tumors, where Src activity is enhanced at the invasive border relative to the tumor cortex. Upon treatment with dasatinib, we observed a switch in activity at the invasive borders, correlating with impaired metastatic capacity in vivo. Src regulation was governed by the proximity of cells to the host vasculature, as cells distal to the vasculature were regulated differentially in response to drug treatment compared with cells proximal to the vasculature. Overall, our results in live tumors revealed that a threshold of drug penetrance exists in vivo and that this can be used to map areas of poor drug-targeting efficiency within specific tumor microenvironments. We propose that using FLIM-FRET in this capacity could provide a useful preclinical tool in animal models before clinical translation. Cancer Res; 73(15); 4674-86. ©2013 AACR.

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[41]
TÍTULO / TITLE: - Paraduodenal Pancreatitis: Clinical Performance of MR Imaging in Distinguishing from Carcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Radiology. 2013 Jul 11.
●● Enlace al texto completo (gratuito o de pago) 1148/radiol.13112056

AUTORES / AUTHORS: - Kalb B; Martin DR; Sarmiento JM; Erickson SH; Gober D; Tapper EB; Chen Z; Adsay NV

INSTITUCIÓN / INSTITUTION: - Department of Radiology, University of Arizona College of Medicine, 1501 N Campbell Ave, Tucson, AZ 85724; Departments of Surgery and Pathology, Emory University School of Medicine, Atlanta, Ga; Department of Radiology, University of Virginia School of Medicine, Charlottesville, Va; Rome Radiology Group, Rome, Ga; Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Mass.

RESUMEN / SUMMARY: - Purpose:To evaluate the diagnostic performance of contrast material-enhanced magnetic resonance (MR) imaging for distinguishing paraduodenal pancreatitis (PDP) from pancreatic head duct adenocarcinoma (CA) in patients with diagnoses confirmed by histopathologic analysis.Materials and Methods:This retrospective study was approved by the institutional review board and is HIPAA compliant. Between July 2007 and July 2010, 47 patients who underwent Whipple procedure and MR imaging less than 60 days before surgery were identified retrospectively. Two relatively inexperienced fellowship trainees with 9 months of body fellowship training were asked to record the presence or absence of three MR imaging features: focal thickening of the second portion of the duodenum; abnormal enhancement of the second portion of the duodenum; and cystic focus in the expected region of the accessory pancreatic duct. Strict criteria for diagnosis of PDP included presence of all three imaging features. Any case that did not fulfill the criteria was classified as CA. Sensitivity, specificity, positive predictive value, and negative predictive value for characterization of PDP was calculated for each reader with 95% confidence intervals. A kappa test assessed level of agreement between readers.Results:Each reader correctly categorized 15 of 17 (88.2%) PDP cases when all three imaging criteria were met. Alternatively, 26 of 30 (86.7%) pancreatic duct CA were correctly categorized as inconsistent with PDP. Four patients with histopathologic diagnosis of CA were incorrectly classified as PDP by each reader. Agreement between the two readers showed substantial kappa agreement for the diagnosis of PDP and differentiation from pancreatic duct CA.Conclusion:Contrast-enhanced MR imaging may help accurately identify PDP and distinguish it from CA when strict diagnostic criteria are followed.© RSNA, 2013Supplemental material: http://radiology.rsna.org/lookup/suppl/doi:10.1148/radiol.13112056/-/DC1.

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[42]

TÍTULO / TITLE: - Extracellular DNA in pancreatic cancer promotes cell invasion and metastasis.

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

REVISTA / JOURNAL: - Cancer Res. 2013 Jul 15;73(14):4256-66. doi: 10.1158/0008-5472.CAN-12-3287. Epub 2013 May 30.

●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-12-3287

AUTORES / AUTHORS: - Wen F; Shen A; Choi A; Gerner EW; Shi J

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Department of Surgery, Arizona Cancer Center; BIO5 Institute and Arizona Cancer Center, BIO5 Oro Valley, University of Arizona, Tucson, Arizona; and Department of Pathology, University of Michigan, Ann Arbor, Michigan.

RESUMEN / SUMMARY: - Aggressive metastasis is the chief cause of the high morbidity and mortality associated with pancreatic cancer, yet the basis for its aggressive behavior remains elusive. Extracellular DNA (exDNA) is a recently discovered component of inflammatory tissue states. Here, we report that exDNA is present on the surface of pancreatic cancer cells where it is critical for driving metastatic behavior. exDNA was abundant on the surface and vicinity of cultured pancreatic cancer cells but absent from normal pancreas cells. Strikingly, treatment of cancer cell cultures with DNase I to degrade DNA nonspecifically reduced metastatic characters associated with matrix attachment, migration, and invasion. We further assessed the role of exDNA in pancreatic cancer metastasis in vivo using an orthotopic xenograft model established by implantation of pancreatic cancer cells expressing firefly luciferase. Noninvasive bioluminescent imaging confirmed that DNase I treatment was sufficient to suppress tumor metastasis. Mechanistic investigations suggested the existence of a positive feedback loop in which exDNA promotes expression of the inflammatory chemokine CXCL8, which leads to higher production of exDNA by pancreatic cancer cells, with a significant reduction in CXCL8 levels achieved by DNase I treatment. Taken together, our results strongly suggest that exDNA contributes to the highly invasive and metastatic character of pancreatic cancer. Cancer Res; 73(14); 4256-66. ©2013 AACR.

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[43]

TÍTULO / TITLE: - Prostate cancer metastatic to the pancreas.

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

REVISTA / JOURNAL: - J Clin Oncol. 2013 Jul 20;31(21):e367-9. doi: 10.1200/JCO.2012.45.1427. Epub 2013 Jun 10.

●● Enlace al texto completo (gratuito o de pago) 1200/JCO.2012.45.1427

AUTORES / AUTHORS: - Wang W; Stroehlein JR; Landon G; Ross WA

INSTITUCIÓN / INSTITUTION: - MBA, Department of Gastroenterology, Hepatology and Nutrition, University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Unit 1466, Houston, TX 77030; wross@mdanderson.org.

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[44]

TÍTULO / TITLE: - Non-hodgkin lymphoma mimicking pancreatic adenocarcinoma and peritoneal carcinomatosis.

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

REVISTA / JOURNAL: - J Clin Oncol. 2013 Jul 20;31(21):e373-6. doi: 10.1200/JCO.2012.45.2904. Epub 2013 Jun 3.

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

1200/JCO.2012.45.2904

AUTORES / AUTHORS: - Fukita Y; Asaki T; Adachi S; Yasuda I; Toyomizu M; Katakura Y

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Seirei Yokohama Hospital, 215 Iwai-cho, Hodogaya-ku, Yokohama, Kanagawa, 240-8521, Japan; yfukita@sis.seirei.or.jp.

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[45]

TÍTULO / TITLE: - Preoperative Gemcitabine-Based Chemoradiation Therapy for Resectable and Borderline Resectable Pancreatic Cancer.

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

REVISTA / JOURNAL: - Ann Surg. 2013 Jun 24.

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

1097/SLA.0b013e31829b3ce4

AUTORES / AUTHORS: - Takahashi H; Ohigashi H; Gotoh K; Marubashi S; Yamada T; Murata M; Ioka T; Uehara H; Yano M; Ishikawa O

INSTITUCIÓN / INSTITUTION: - Departments of *Surgery daggerDiagnostic Radiology double daggerCancer Survey section signGastroenterology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan.

RESUMEN / SUMMARY: - OBJECTIVE:: To evaluate the outcome of preoperative gemcitabine-based chemoradiation therapy (CRT) for resectable and borderline resectable pancreatic cancer (PC), with a focus on the differences in surgical outcomes and patterns of recurrence between these 2 categories. BACKGROUND:: Various multimodal treatment strategies have been proposed to improve the surgical outcomes of PC. Preoperative CRT and subsequent surgery is one of the promising strategies for resectable (PC-R) and borderline resectable (PC-BR) PC. METHODS:: A total of 268 patients with PC-R and PC-BR received preoperative gemcitabine-based CRT. The numbers of PC-R and PC-BR cases were 188 and 80, respectively. We evaluated the following comparisons between patients with PC-R and those with PC-BR: (1) resection rate, (2) rate of margin-negative resection, (3) survival, and (4) pattern of the treatment failure, including local recurrence, peritoneal dissemination, and distant metastasis. RESULTS:: The resection rate of patients with PC-R (87%) was higher than that of patients with PC-BR (54%) ($P < 0.001$). Pathological margin-negative resection was achieved in 99% and 98% of the patients with PC-R and PC-BR, respectively. The 5-year survival rates of the PC-R and PC-BR cases were 57% and 34%, respectively ($P = 0.029$). Although the 5-year

cumulative incidence of local recurrence was comparable in both groups (15% and 13%, respectively; P = 0.508), the 5-year cumulative incidence of peritoneal and distant recurrence was significantly higher in the patients with PC-BR (43 and 76%) than in the patients with PC-R (17% and 43%). CONCLUSIONS:: In the resected cases, the locoregional control was comparable between patients with PC-R and PC-BR after preoperative CRT. The survival rate for the patients with PC-BR was lower than the rate for those with PC-R due to a higher incidence of peritoneal and distant recurrence in the patients with PC-BR. (UMIN000001804).

PTPTPTP - JOURNAL ARTICLE ---------- [46]

TÍTULO / TITLE: - Tumor Recurrence Is Independent of Pancreatic Fistula in Patients after Pancreaticoduodenectomy for Pancreatic Ductal Adenocarcinoma.

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

REVISTA / JOURNAL: - J Am Coll Surg. 2013 Jun 27. pii: S1072-7515(13)00401-8. doi: 10.1016/j.jamcollsurg.2013.05.014.

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

1016/j.jamcollsurg.2013.05.014

AUTORES / AUTHORS: - Assifi MM; Zhang S; Leiby BE; Pequignot EC; Xia B; Rosato E; Lavu H; Kennedy EP; Yeo CJ; Berger AC

INSTITUCIÓN / INSTITUTION: - Department of Surgery and the Jefferson Pancreas, Biliary and Related Cancer Center, Thomas Jefferson University, Philadelphia, PA.

RESUMEN / SUMMARY: - BACKGROUND: Recurrence of pancreatic adenocarcinoma after pancreaticoduodenectomy (PD) can be increased in patients with pancreatic fistula (PF). The purpose of our study was to determine if a relationship exists between PF and tumor recurrence (both peritoneal and local) in patients after PD for pancreatic ductal adenocarcinoma. STUDY DESIGN: A single-institution, retrospective analysis of 221 patients who underwent PD from January 2001 to December 2009 was conducted. Electronic charts and medical records were queried for tumor characteristics, recurrence, and complications. Presence and grading of PF was determined using the criteria of the International Study Group on Pancreatic Fistula. Data were analyzed using chi-square and Kaplan-Meier survival statistics. RESULTS: There were 114 male and 107 female patients. Mean age was 66 years (range 35 to 91 years). The vast majority (84%) of patients had stage II disease; 143 (65%) had positive lymph nodes (median 2 positive nodes; range 1 to 17 positive nodes). Pancreatic fistula developed in 23 patients (grade A, n = 9; grade B, n = 13; grade C, n = 1; 10.2%). Peritoneal recurrence was noted in 20 patients (9%). Of the 23 patients with PF, peritoneal recurrence developed in 3 (13%). Of the 198 patients without PF, peritoneal recurrence developed in 17 (10%). Local recurrence occurred in 47 patients (21%), 5 (2%) in patients with PF and 42 (21%) in those without PF (p = NS). In Kaplan-Meier survival

analysis, there was no significant difference in recurrence-free survival (p = 0.4) and overall survival (p = 0.3) for those with PF vs those without PF. CONCLUSIONS: Patients with PF after PD were not found to have a significant increase in local or peritoneal recurrence. Therefore, in this analysis, postoperative PF does not appear to serve as an adverse prognostic marker.

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[47]

TÍTULO / TITLE: - Canonical Wnt Signaling Is Required for Pancreatic Carcinogenesis.

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

REVISTA / JOURNAL: - Cancer Res. 2013 Aug 1;73(15):4909-4922. Epub 2013 Jun 12.

●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-12-4384

AUTORES / AUTHORS: - Zhang Y; Morris JP 4th; Yan W; Schofield HK; Gurney A; Simeone DM; Millar SE; Hoey T; Hebrok M; Pasca di Magliano M

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of Surgery, Pathology, Molecular and Integrative Physiology, and Cell and Developmental Biology; Michigan Center for Translational Pathology; Medical Scientist Training Program; Comprehensive Cancer Center, University of Michigan Medical School, Ann Arbor, Michigan; Diabetes Center, University of California, San Francisco, San Francisco; OncoMed Pharmaceutical, Redwood City, California; Departments of Dermatology, and Cell and Developmental Biology, University of Pennsylvania, Philadelphia, Pennsylvania.

RESUMEN / SUMMARY: - Wnt ligand expression and activation of the Wnt/beta-catenin pathway have been associated with pancreatic ductal adenocarcinoma, but whether Wnt activity is required for the development of pancreatic cancer has remained unclear. Here, we report the results of three different approaches to inhibit the Wnt/beta-catenin pathway in a established transgenic mouse model of pancreatic cancer. First, we found that beta-catenin null cells were incapable of undergoing acinar to ductal metaplasia, a process associated with development of premalignant pancreatic intraepithelial neoplasia lesions. Second, we addressed the specific role of ligand-mediated Wnt signaling through inducible expression of Dkk1, an endogenous secreted inhibitor of the canonical Wnt pathway. Finally, we targeted the Wnt pathway with OMP-18R5, a therapeutic antibody that interacts with multiple Frizzled receptors. Together, these approaches showed that ligand-mediated activation of the Wnt/beta-catenin pathway is required to initiate pancreatic cancer. Moreover, they establish that Wnt signaling is also critical for progression of pancreatic cancer, a finding with potential therapeutic implications. Cancer Res; 73(15); 4909-22. ©2013 AACR.

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[48]
TÍTULO / TITLE: - PanIN-Specific Regulation of Wnt Signaling by HIF2alpha during Early Pancreatic Tumorigenesis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cancer Res. 2013 Aug 1;73(15):4781-4790. Epub 2013 Jun 7.
●● Enlace al texto completo (gratuito o de pago) 1158/0008-5472.CAN-13-0566
AUTORES / AUTHORS: - Criscimanna A; Duan LJ; Rhodes JA; Fendrich V; Wickline E; Hartman DJ; Monga SP; Lotze MT; Gittes GK; Fong GH; Esni F
INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Division of Pediatric General and Thoracic Surgery, Department of Surgery, Children's Hospital of Pittsburgh, University of Pittsburgh Medical Center; Departments of Pathology, Developmental Biology, and Microbiology and Molecular Genetics, University of Pittsburgh; University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania; Center for Vascular Biology, Department of Cell Biology, University of Connecticut Health Center, Farmington, Connecticut; and Department of Surgery, Philipps University Marburg, Baldingerstrasse, Marburg, Germany.
RESUMEN / SUMMARY: - Hypoxia promotes angiogenesis, proliferation, invasion, and metastasis of pancreatic cancer. Essentially, all studies of the hypoxia pathway in pancreatic cancer research to date have focused on fully malignant tumors or cancer cell lines, but the potential role of hypoxia inducible factors (HIF) in the progression of premalignant lesions has not been critically examined. Here, we show that HIF2alpha is expressed early in pancreatic lesions both in human and in a mouse model of pancreatic cancer. HIF2alpha is a potent oncogenic stimulus, but its role in Kras-induced pancreatic neoplasia has not been discerned. We used the Ptf1aCre transgene to activate KrasG12D and delete Hif2alpha solely within the pancreas. Surprisingly, loss of Hif2alpha in this model led to markedly higher, rather than reduced, number of low-grade pancreatic intraepithelial neoplasia (mPanIN) lesions. These lesions, however, failed to progress to high-grade mPanINs, and displayed exclusive loss of beta-catenin and SMAD4. The relationship among HIF2alpha, beta-catenin, and Smad4 was further confirmed in vitro, where silencing of Hif2alpha resulted in reduced beta-catenin and Smad4 transcript levels. Thus, with oncogenic Ras expressed in the pancreas, HIF2alpha modulates Wnt-signaling during mPanIN progression by maintaining appropriate levels of both Smad4 and beta-catenin. Cancer Res; 73(15); 4781-90. ©2013 AACR.

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[49]
TÍTULO / TITLE: - Clinical and Morphological Characteristics of Sporadic Genetically Determined Pancreatitis as Compared to Idiopathic Pancreatitis: Higher Risk of Pancreatic Cancer in CFTR Variants.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Digestion. 2013;87(4):229-39. doi: 10.1159/000348439. Epub 2013 Jun 4.

●● Enlace al texto completo (gratuito o de pago) 1159/000348439

AUTORES / AUTHORS: - Hamoir C; Pepermans X; Piessevaux H; Jouret-Mourin A; Weynand B; Habyalimana JB; Leal T; Geubel A; Gigot JF; Deprez PH

INSTITUCIÓN / INSTITUTION: - Hepato-Gastroenterology Department, Cliniques universitaires Saint-Luc, Universite Catholique de Louvain, Brussels, Belgium.

RESUMEN / SUMMARY: - Background/Aims: Idiopathic pancreatitis is considered to be a multigenic and multifactorial disease. Genetically determined pancreatitis is associated with mutations in the PRSS1,SPINK1 and CFTR genes. This study aimed at examining the clinical and morphological characteristics of patients diagnosed with genetically determined sporadic pancreatitis. Methods: Inclusion criteria were the presence of PRSS1,CFTR or SPINK1 gene mutations in patients with idiopathic recurrent or chronic pancreatitis. Patients with hereditary pancreatitis were excluded. Age- and sex-matched patients with idiopathic pancreatitis and negative genetic testing served as controls (n = 68). Results: Genetic testing was performed in 351 probands referred to our centre since 1999. Sixty-one patients (17.4%) carried at least 1 detected mutation in 1 of the 3 tested genes (34 CFTR, 10 PRSS1 and 13 SPINK1 mutations), and 4 patients showed a combination of mutations. Follow-up has been currently extended to a median of 5 years (range 1-40). Similar clinical features were noted in the case and matched groups except for an earlier age of onset of pancreatic symptoms and a higher incidence of pancreatic cancer in the case group and in patients with CFTR mutations compared to the control group ($p < 0.05$). The standardized incidence ratio, the ratio of observed to expected pancreatic cancers, averaged 26.5 (95% confidence interval 8.6-61.9). All pancreatic cancer patients were smokers. Conclusion: Clinical parameters of patients with sporadic idiopathic pancreatitis and gene mutations are similar to those of age- and sex-matched patients without gene mutations, except for the age of pancreatic disease onset. A significantly higher occurrence of pancreas cancer was observed in the case group, particularly in those patients carrying CFTR mutations. We therefore suggest to include patients with CFTR variants presenting with risk factors in a screening and surveillance programme and to strongly advise them to stop smoking.

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[50]

TÍTULO / TITLE: - Multifunctional roles of Urokinase Plasminogen Activator (uPA) in Cancer Stemness and in Chemo-resistance of Pancreatic Cancer.

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

REVISTA / JOURNAL: - Mol Biol Cell. 2013 Jul 17.

●● Enlace al texto completo (gratuito o de pago) 1091/mbc.E12-04-0306

AUTORES / AUTHORS: - Asuthkar S; Stepanova V; Lebedeva T; Holterman AL; Estes N; Cines DB; Rao JS; Gondi CS

INSTITUCIÓN / INSTITUTION: - Department of Cancer Biology and Pharmacology, University of Illinois College of Medicine at Peoria, Peoria, IL, USA Department of Pathology and Laboratory Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA Department of Surgery University of Illinois College of Medicine at Peoria, Peoria, IL, USA Department of Medicine, University of Illinois College of Medicine at Peoria, Peoria, IL, USA.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is almost lethal. One of the underlying reasons for this lethality is thought to be the presence of cancer stem cells (CSC), which impart chemo-resistance and promote recurrence, but the mechanisms responsible for this biology are unclear. Recently the poor prognosis of PDAC has been correlated with increased expression of urokinase plasminogen activator (uPA). Therefore, in the present study we examined the role of uPA in the generation of PDAC-CSC. We observed a subset of cells identifiable as a side-population (SP) when sorted by flow-cytrometry of MIA PaCa-2 and PANC-1 pancreatic cancer cells that possessed the properties of CSC. A large fraction of these SP cells were CD44- and CD24-positive, were gemcitabine resistant, possess sphere forming ability and exhibit increased tumorogenisity, which are known characteristic of cancer stemness. Increased tumorogenisity and gemcitabine resistance was decreased after suppression of uPA. We observed that uPA interacts directly with transcription factors Lhx-2, HOXA5 and Hey to possibly promote cancer stemness. uPA regulates Lhx-2 expression by suppressing expression of miR-124, and p53 expression by repressing its promoter by inactivating HOXA5. These results demonstrate that regulation of gene transcription by uPA contributes to cancer stemness and clinical lethality.

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[51]

TÍTULO / TITLE: - An Undesired Effect of Chemotherapy: GEMCITABINE PROMOTES PANCREATIC CANCER CELL INVASIVENESS THROUGH REACTIVE OXYGEN SPECIES-DEPENDENT, NUCLEAR FACTOR kappaB- AND HYPOXIA-INDUCIBLE FACTOR 1alpha-MEDIATED UP-REGULATION OF CXCR4.

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

REVISTA / JOURNAL: - J Biol Chem. 2013 Jul 19;288(29):21197-207. doi: 10.1074/jbc.M113.484576. Epub 2013 Jun 5.

●● Enlace al texto completo (gratuito o de pago) 1074/jbc.M113.484576

AUTORES / AUTHORS: - Arora S; Bhardwaj A; Singh S; Srivastava SK; McClellan S; Nirodi CS; Piazza GA; Grizzle WE; Owen LB; Singh AP

INSTITUCIÓN / INSTITUTION: - From the Department of Oncologic Sciences, Mitchell Cancer Institute, University of South Alabama, Mobile, Alabama 36604.

RESUMEN / SUMMARY: - Recently, we have shown that CXCL12/CXCR4 signaling plays an important role in gemcitabine resistance of pancreatic cancer (PC) cells. Here, we explored the effect of gemcitabine on this resistance mechanism. Our data demonstrate that gemcitabine induces CXCR4 expression in two PC cell lines (MiaPaCa and Colo357) in a dose- and time-dependent manner. Gemcitabine-induced CXCR4 expression is dependent on reactive oxygen species (ROS) generation because it is abrogated by pretreatment of PC cells with the free radical scavenger N-acetyl-L-cysteine. CXCR4 up-regulation by gemcitabine correlates with time-dependent accumulation of NF-kappaB and HIF-1alpha in the nucleus. Enhanced binding of NF-kappaB and HIF-1alpha to the CXCR4 promoter is observed in gemcitabine-treated PC cells, whereas their silencing by RNA interference causes suppression of gemcitabine-induced CXCR4 expression. ROS induction upon gemcitabine treatment precedes the nuclear accumulation of NF-kappaB and HIF-1alpha, and suppression of ROS diminishes these effects. The effect of ROS on NF-kappaB and HIF-1alpha is mediated through activation of ERK1/2 and Akt, and their pharmacological inhibition also suppresses gemcitabine-induced CXCR4 up-regulation. Interestingly, our data demonstrate that nuclear accumulation of NF-kappaB results from phosphorylation-induced degradation of IkappaBalpha, whereas HIF-1alpha up-regulation is NF-kappaB-dependent. Lastly, our data demonstrate that gemcitabine-treated PC cells are more motile and exhibit significantly greater invasiveness against a CXCL12 gradient. Together, these findings reinforce the role of CXCL12/CXCR4 signaling in gemcitabine resistance and point toward an unintended and undesired effect of chemotherapy.

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[52]

TÍTULO / TITLE: - Tumor Protein D52 Controls Trafficking of an Apical Endolysosomal Secretory Pathway in Pancreatic Acinar Cells.

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

REVISTA / JOURNAL: - Am J Physiol Gastrointest Liver Physiol. 2013 Jul 18.

●● Enlace al texto completo (gratuito o de pago) 1152/ajpgi.00143.2013

AUTORES / AUTHORS: - Messenger SW; Thomas DD; Falkowski MA; Byrne JA; Gorelick FS; Groblewski GE

INSTITUCIÓN / INSTITUTION: - 1University of Wisconsin.

RESUMEN / SUMMARY: - Zymogen granule (ZG) formation in acinar cells involves zymogen-cargo sorting from trans-Golgi into immature secretory granules (ISGs). ISG maturation progresses by removal of lysosomal membrane and select-content proteins which enter endosomal intermediates prior to their apical exocytosis. Constitutive and stimulated secretion through this mechanism is termed the constitutive-like (CLP) and minor-regulated (MRP) pathways, respectfully. However, the molecular components that control membrane trafficking within these endosomal compartments are unknown. We show that

tumor protein D52 is highly expressed in endosomal compartments following pancreatic acinar stimulation and regulates apical exocytosis of an apically directed endolysosomal compartment. Secretion from the endolysosomal compartment was detected by cell-surface labeling of lysosome associated membrane protein LAMP1, which is absent from ZGs, and had incomplete overlap with surface labeling of synaptotagmin, a marker of ZG exocytosis. Although culturing (16-18 h) of isolated acinar cells is accompanied by a loss of secretory responsiveness, levels of SNARE proteins necessary for ZG exocytosis were preserved. However, levels of endolysosomal proteins D52, EEA1, Rab5 and LAMP1 markedly decreased. When D52 levels were restored by adenoviral delivery, the levels of these regulatory proteins and secretion of both LAMP1 (endolysosomal) and amylase was strongly enhanced. These secretory effects were absent in alanine and aspartate substitutions of serine 136, the major D52 phosphorylation site, and were inhibited by brefeldin A, which does not directly affect the ZG compartment. Results indicate D52 directly regulates apical endolysosomal secretion and are consistent with previous studies suggesting this pathway indirectly regulates ZG secretion of digestive enzymes.

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[53]

TÍTULO / TITLE: - Pancreatic Cancer Risk After Loss of a Child: A Register-based Study in Sweden During 1991-2009.

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

REVISTA / JOURNAL: - Am J Epidemiol. 2013 Aug 15;178(4):582-9. doi: 10.1093/aje/kwt045. Epub 2013 Jun 20.

●● Enlace al texto completo (gratuito o de pago) 1093/aje/kwt045

AUTORES / AUTHORS: - Huang J; Valdimarsdottir U; Fall K; Ye W; Fang F

RESUMEN / SUMMARY: - The potential role of psychological stress in pancreatic cancer has rarely been investigated in epidemiologic studies. During 1991-2009, we conducted a nested case-control study based on Swedish national population and health registers to investigate whether severe psychological stress induced by the death of a child was associated with subsequent risk of pancreatic cancer. The study included 16,522 cases and 82,107 controls who were matched to the cases on sex and year of birth. Conditional logistic regression was used to estimate odds ratios and 95% confidence intervals. Overall, loss of a child was associated with an odds ratio of 1.09 for pancreatic cancer (95% confidence interval (CI): 1.02, 1.17). The risk elevation was mainly seen during the first 5 years after the loss (odds ratio (OR) = 1.27, 95% CI: 1.12, 1.45) and for loss of a child due to suicide (OR = 1.23, 95% CI: 1.03, 1.46). The association was statistically significant among women but not among men, and it appeared stronger for early-onset pancreatic cancer. Persons with a history of psychiatric illness had the greatest risk increase after child loss (OR = 1.43, 95% CI: 1.17, 1.76). Although other explanations are

possible, our findings provide some evidence that psychological stress may be associated with pancreatic cancer.

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[54]

TÍTULO / TITLE: - Activated PAR-2 Regulates Pancreatic Cancer Progression through ILK/HIF-alpha-Induced TGF-alpha Expression and MEK/VEGF-A-Mediated Angiogenesis.

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

REVISTA / JOURNAL: - Am J Pathol. 2013 Aug;183(2):566-75. doi: 10.1016/j.ajpath.2013.04.022. Epub 2013 Jun 10.

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

1016/j.ajpath.2013.04.022

AUTORES / AUTHORS: - Chang LH; Pan SL; Lai CY; Tsai AC; Teng CM

INSTITUCIÓN / INSTITUTION: - Pharmacological Institute, College of Medicine, National Taiwan University, Taipei, Taiwan.

RESUMEN / SUMMARY: - Tissue factor initiates the process of thrombosis and activates cell signaling through protease-activated receptor-2 (PAR-2). The aim of this study was to investigate the pathological role of PAR-2 signaling in pancreatic cancer. We first demonstrated that activated PAR-2 up-regulated the protein expression of both hypoxia-inducible factor-1alpha (HIF-1alpha) and HIF-2alpha, resulting in enhanced transcription of transforming growth factor-alpha (TGF-alpha). Down-regulation of HIFs-alpha by siRNA or YC-1, an HIF inhibitor, resulted in depleted levels of TGF-alpha protein. Furthermore, PAR-2, through integrin-linked kinase (ILK) signaling, including the p-AKT, promoted HIF protein expression. Diminishing ILK by siRNA decreased the levels of PAR-2-induced p-AKT, HIFs-alpha, and TGF-alpha; our results suggest that ILK is involved in the PAR-2-mediated TGF-alpha via an HIF-alpha-dependent pathway. Furthermore, the culture medium from PAR-2-treated pancreatic cancer cells enhanced human umbilical vein endothelial cell proliferation and tube formation, which was blocked by the MEK inhibitor, PD98059. We also found that activated PAR-2 enhanced tumor angiogenesis through the release of vascular endothelial growth factor-A (VEGF-A) from cancer cells, independent of the ILK/HIFs-alpha pathways. Consistent with microarray analysis, activated PAR-2 induced TGF-A and VEGF-A gene expression. In conclusion, the activation of PAR-2 signaling induced human pancreatic cancer progression through the induction of TGF-alpha expression by ILK/HIFs-alpha, as well as through MEK/VEGF-A-mediated angiogenesis, and it plays a role in the interaction between cancer progression and cancer-related thrombosis.

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[55]

TÍTULO / TITLE: - Expression of core 3 synthase in human pancreatic cancer cells suppresses tumor growth and metastasis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Int J Cancer. 2013 Jun 10. doi: 10.1002/ijc.28322.
●● Enlace al texto completo (gratuito o de pago) 1002/ijc.28322
AUTORES / AUTHORS: - Radhakrishnan P; Grandgenett PM; Mohr AM; Bunt SK; Yu F; Chowdhury S; Hollingsworth MA
INSTITUCIÓN / INSTITUTION: - Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, NE.
RESUMEN / SUMMARY: - Core 3-derived glycans, a major type of O-glycan expressed by normal epithelial cells of the gastrointestinal tract, are downregulated during malignancy because of loss of expression of functional beta3-N-acetylglucosaminyltransferase-6 (core 3 synthase). We investigated the expression of core 3 synthase in normal pancreas and pancreatic cancer and evaluated the biological effects of re-expressing core 3 synthase in pancreatic cancer cells that had lost expression. We determined that pancreatic tumors and tumor cell lines have lost expression of core 3 synthase. Therefore, we re-expressed core 3 synthase in human pancreatic cancer cells (Capan-2 and FG) to investigate the contribution of core 3 glycans to malignant progression. Pancreatic cancer cells expressing core 3 synthase showed reduced in vitro cell proliferation, migration and invasion compared to vector control cells. Expression of core 3 O-glycans induced altered expression of beta1 integrin, decreased activation of focal adhesion kinase, led to the downregulation of expression of several genes including REG1alpha and FGFR3 and altered lamellipodia formation. The addition of a GlcNAc residue by core 3 synthase leads to the extension of the tumor-associated Tn structure on MUC1. Orthotopic injection of FG cells expressing core 3 synthase into the pancreas of nude mice produced significantly smaller tumors and decreased metastasis to the surrounding tissues compared to vector control FG cells. These findings indicate that expression of core 3-derived O-glycans in pancreatic cancer cells suppresses tumor growth and metastasis through modulation of glycosylation of mucins and other cell surface and extracellular matrix proteins.

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[56]
TÍTULO / TITLE: - Incretins and risk of neoplasia.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - BMJ. 2013 Jun 10;346:f3750. doi: 10.1136/bmj.f3750.
AUTORES / AUTHORS: - Halfdanarson TR; Pannala R
INSTITUCIÓN / INSTITUTION: - Division of Hematology and Oncology, Mayo Clinic, Scottsdale, AZ 85259, USA. thorvardur.halfdanarson@mayo.edu

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[57]

TÍTULO / TITLE: - Up-regulation of DDX39 in Human Pancreatic Cancer Cells with Acquired Gemcitabine Resistance Compared to Gemcitabine-sensitive Parental Cells.

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

REVISTA / JOURNAL: - Anticancer Res. 2013 Aug;33(8):3133-6.

AUTORES / AUTHORS: - Kuramitsu Y; Suenaga S; Wang Y; Tokuda K; Kitagawa T; Tanaka T; Akada J; Maehara S; Maehara Y; Nakamura K

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

RESUMEN / SUMMARY: - Intrinsic or acquired resistance of pancreatic cancer to gemcitabine (2'-deoxy-2'-difluorodeoxycytidine) is an important factor in the failure of gemcitabine treatment. Proteomic analysis of gemcitabine-sensitive KLM1 pancreatic cancer cells and -resistant KLM1-R cells identified heat-shock protein-27(HSP27) as a biomarker protein which is involved in gemcitabine resistance. However, a knock-down experiment showed that HSP27 was not the only protein implicated with gemcitabine-resistance. Finding further candidate proteins is necessary for achieving effective gemcitabine therapy for patients with pancreatic cancer. DDX39 is an Asp-Glu-Ala-Asp (DEAD)-box RNA helicase reported to be overexpressed in tumor cells, such as lung squamous cell cancer, gastrointestinal stromal tumor, urinary bladder cancer and malignant pleural mesothelioma. In urinary bladder cancer cells, overexpression of this protein is intimately bound with tumorigenesis and poor prognosis. In the present study, the expression of DDX39 in gemcitabine-sensitive KLM1 and -resistant KLM1-R cells was compared. It was found that DDX39 was significantly up-regulated in gemcitabine-resistant KLM1-R cells compared to sensitive KLM1 cells. The ratio of expression of DDX39 to that of actin was significantly up-regulated in KLM1-R cells compared to KLM1 cells ($p=0.0072$ by Student's t-test). These results suggest that DDX39 is a possible candidate biomarker for predicting the response of patients with pancreatic cancer to treatment with gemcitabine.

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[58]

TÍTULO / TITLE: - Clinical impact of pentraxin family expression on prognosis of pancreatic carcinoma.

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

REVISTA / JOURNAL: - Br J Cancer. 2013 Aug 6;109(3):739-46. doi: 10.1038/bjc.2013.348. Epub 2013 Jul 4.

●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.348

AUTORES / AUTHORS: - Kondo S; Ueno H; Hosoi H; Hashimoto J; Morizane C; Koizumi F; Tamura K; Okusaka T

INSTITUCIÓN / INSTITUTION: - Division of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital, 5-1-1 Tsukiji Chuo-ku, Tokyo 104-0045, Japan.

RESUMEN / SUMMARY: - Background:Inflammatory mediators may have decisive roles at different stages of tumour development. Mediators within the pentraxin family may be used as strong biomarkers in prognosis of advanced pancreatic carcinoma patients.Methods:Using pancreatic carcinoma cell lines and gene transfectant, we measured long pentraxin (PTX3) level in culture solution and carried out cellular migration assay in vitro. In vivo study of the treatment-naive patients with advanced pancreatic carcinoma assigned to undergo gemcitabine therapy was prospectively conducted to measure and investigate the role of plasma PTX3, C-reactive protein (CRP), and eight inflammatory mediators by using collected clinical data.Results:Elevated PTX3 production was observed in several cell lines, and a direct relationship between migratory activity and PTX3 level was identified in vitro. High PTX3 level (117 days) was significantly less than that of patients with low PTX3 level (357 days, P<0.001). Multivariate analysis of the pancreatic carcinoma revealed a strong correlation between pentraxin family member expression and prognosis of pancreatic carcinoma. The relationship between PTX3 expression and the expression of other pro-inflammatory mediators indicated that PTX3 level is positively correlated with levels of CRP, interleukin-6, and macrophage-inhibitory factor.Conclusion:Pentraxin family members, especially PTX3, may be used as promising biomarkers in the prognosis of pancreatic carcinoma patients.

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[59]

TÍTULO / TITLE: - Clinico-pathological characteristics and clinical outcome of different histological types of pancreatic cancer in a large Middle European series.

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

REVISTA / JOURNAL: - J Clin Pathol. 2013 Jun 8.

●● Enlace al texto completo (gratuito o de pago) 1136/jclinpath-2012-201394

AUTORES / AUTHORS: - Stotz M; Eisner F; Szkandera J; Absenger G; Kornprat P; Lackner C; Samonigg H; Gerger A; Pichler M

INSTITUCIÓN / INSTITUTION: - Division of Oncology, Department of Internal Medicine, Medical University of Graz, Graz, Austria.

RESUMEN / SUMMARY: - AIMS: Pancreatic cancer (PC) is a heterogeneous disease in terms of histological and molecular subtypes. The aim of this study was to evaluate the prognostic impact of different histological subtypes on cancer-specific survival (CSS) in a large single-centre Middle European cohort. METHODS: We retrospectively studied the records of 400 consecutive PC patients who were treated from 2004 to 2010 at a single tertiary academic centre. The association of histological subtypes and parameters such as tumour

stage, tumour grade, levels of tumour markers carcinoembryonic antigen and CA19-9 at diagnosis, was studied. CSS was calculated using the Kaplan-Meier method, and the influence of each parameter on CSS was assessed with univariate and multivariable Cox proportional models. RESULTS: The survival time was significantly shorter in the ductal adenocarcinoma and acinar histological subtypes compared to neuroendocrine differentiation (p<0.001). No survival difference was observed between ductal adenocarcinomas and patients with a histological variant of ductal adenocarcinoma, namely, mucinous non-cystic adenocarcinoma (p=0.7). In multivariable analysis, ductal adenocarcinoma (HR=3.1, CI 1.6 to 6.1, p=0.001) and acinar carcinoma (HR=3.2, CI 1.3 to 8.5, p=0.016) were identified as independent predictors for CSS. CONCLUSIONS: Our findings suggest that the main histological subtype is an independent predictor of CSS in patients with PC. Thus, our data underline the importance of routine assessment of histological type in PC for individual risk assessment. However, no clinical rationale for the subdivision of ductal adenocarcinoma and mucinous non-cystic adenocarcinoma can be supported by our study.

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[60]

TÍTULO / TITLE: - Allergies and Risk of Pancreatic Cancer: A Pooled Analysis From the Pancreatic Cancer Case-Control Consortium.

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

REVISTA / JOURNAL: - Am J Epidemiol. 2013 Jul 2.

●● Enlace al texto completo (gratuito o de pago) 1093/aje/kwt052

AUTORES / AUTHORS: - Olson SH; Hsu M; Satagopan JM; Maisonneuve P; Silverman DT; Lucenteforte E; Anderson KE; Borgida A; Bracci PM; Bueno-de-Mesquita HB; Cotterchio M; Dai Q; Duell EJ; Fontham EH; Gallinger S; Holly EA; Ji BT; Kurtz RC; La Vecchia C; Lowenfels AB; Luckett B; Ludwig E; Petersen GM; Polesel J; Seminara D; Strayer L; Talamini R

RESUMEN / SUMMARY: - In order to quantify the risk of pancreatic cancer associated with history of any allergy and specific allergies, to investigate differences in the association with risk according to age, gender, smoking status, or body mass index, and to study the influence of age at onset, we pooled data from 10 case-control studies. In total, there were 3,567 cases and 9,145 controls. Study-specific odds ratios and 95% confidence intervals were calculated by using unconditional logistic regression adjusted for age, gender, smoking status, and body mass index. Between-study heterogeneity was assessed by using the Cochran Q statistic. Study-specific odds ratios were pooled by using a random-effects model. The odds ratio for any allergy was 0.79 (95% confidence interval (CI): 0.62, 1.00) with heterogeneity among studies (P < 0.001). Heterogeneity was attributable to one study; with that study excluded, the pooled odds ratio was 0.73 (95% CI: 0.64, 0.84) (Pheterogeneity = 0.23). Hay fever (odds ratio = 0.74, 95% CI: 0.56, 0.96) and allergy to

animals (odds ratio = 0.62, 95% CI: 0.41, 0.94) were related to lower risk, while there was no statistically significant association with other allergies or asthma. There were no major differences among subgroups defined by age, gender, smoking status, or body mass index. Older age at onset of allergies was slightly more protective than earlier age.

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[61]

TÍTULO / TITLE: - M2-polarized tumor-associated macrophages promoted epithelial-mesenchymal transition in pancreatic cancer cells, partially through TLR4/IL-10 signaling pathway.

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

REVISTA / JOURNAL: - Lab Invest. 2013 Jul;93(7):844-54. doi: 10.1038/labinvest.2013.69. Epub 2013 Jun 10.

●● Enlace al texto completo (gratuito o de pago) 1038/labinvest.2013.69

AUTORES / AUTHORS: - Liu CY; Xu JY; Shi XY; Huang W; Ruan TY; Xie P; Ding JL

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Wuxi People's Hospital, Affiliated to Nanjing Medical University, Wuxi, PRC.

RESUMEN / SUMMARY: - M2-polarized tumor-associated macrophages (TAMs) are key regulators of the link between inflammation and cancer. A negative correlation between infiltration intensity of M2-polarized TAMs and prognosis of pancreatic cancer has been reported. Epithelial-mesenchymal transition (EMT) is an important biological process in the progression of primary tumors toward metastasis. Inflammation-induced EMT has been previously shown, therefore, we hypothesized M2-polarized TAMs could induce EMT in pancreatic cancer. Toll-like receptor 4 (TLR4) signaling has an active role in tumor progression during chronic inflammation and the receptor is primarily expressed on macrophages. Activation of TLR4 on M2-polarized TAMs stimulates an increase in the cytokine interleukin-10 (IL-10); consequently, another aim was to investigate the potential role of TLR4/IL-10 signaling in the EMT of pancreatic cancer. Treatment with IL-4 (20 ng/ml) for 24 h successfully induced the polarization of macrophage cell line RAW 264.7 to M2 phenotype, IL-10(high), IL-12(low), and IL-23(low), and high expression of CD204 and CD206. A coculture system allowed investigation of the roles of M2-polarized TAMs and TLR4/IL-10 signaling in the EMT of Panc-1 and BxPC-3 pancreatic cancer cell lines. Our results showed that coculture with M2-polarized TAMs increased fibroblastic morphology, upregulated mesenchymal markers vimentin and snail at the mRNA and protein levels, and increased proliferation, migration, and metalloproteinase (MMP)2 and MMP9 proteolytic activity in pancreatic cancer cells. Simultaneously, coculture with M2-polarized TAMs decreased the expression of the epithelial marker E-cadherin. Coculture with pancreatic cancer cells increased TLR4 mRNA and protein expression in M2-polarized TAMs. Application of TLR4 siRNA and neutralizing antibodies against TLR4 and IL-10

markedly inhibited E-cadherin reduction and the upregulation of snail and vimentin. Furthermore, activation of TLR4 signaling by lipopolysaccharide profoundly increased the EMT of pancreatic cancer cells. In conclusion, M2-polarized TAMs promoted EMT in pancreatic cancer cells partially through TLR4/IL-10 signaling, suggesting novel therapeutic strategies and enhancing our understanding of M2-polarized TAMs.

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[62]

TÍTULO / TITLE: - Role of pancreatic cancer-derived exosomes in salivary biomarker development.

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

REVISTA / JOURNAL: - J Biol Chem. 2013 Jul 23.

●● Enlace al texto completo (gratuito o de pago) 1074/jbc.M113.452458

AUTORES / AUTHORS: - Lau C; Kim Y; Chia D; Spielmann N; Eibl G; Elashoff D; Wei F; Lin YL; Moro A; Grogan T; Chiang S; Feinstein E; Schafer C; Farrell J; Wong DT

INSTITUCIÓN / INSTITUTION: - UCLA, United States;

RESUMEN / SUMMARY: - Recent studies have demonstrated that discriminatory salivary biomarkers can be readily detected upon the development of systemic diseases such as pancreatic cancer, breast cancer, lung cancer and ovarian cancer. However, the utility of salivary biomarkers for the detection of systemic diseases has been undermined due to the absence of biological and mechanistic rationale to why distal diseases from the oral cavity would lead to the development of discriminatory biomarkers in saliva. Here, we examine the hypothesis that pancreatic tumor-derived exosomes are mechanistically involved in the development of pancreatic cancer-discriminatory salivary transcriptomic biomarkers. We first developed a pancreatic cancer mouse model that yielded discriminatory salivary biomarkers by implanting the mouse pancreatic cancer cell line Pan02 into the pancreas of the syngeneic host C57BL/6. The role of pancreatic cancer-derived exosomes in the development of discriminatory salivary biomarkers was then tested by engineered a Pan02 cell line that is suppressed for exosome biogenesis, implanted into the C56BL/6 mouse and examine if the discriminatory salivary biomarker profile was ablated or disrupted. Suppression of exosome biogenesis results in the ablation of discriminatory salivary biomarker development. This study supports that tumor-derived exosomes provide a mechanism in the development of discriminatory biomarkers in saliva and distal systemic diseases.

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[63]

TÍTULO / TITLE: - PARP-1 regulates resistance of pancreatic cancer to TRAIL therapy.

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

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

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-0516

AUTORES / AUTHORS: - Yuan K; Sun Y; Zhou T; McDonald JM; Chen Y

INSTITUCIÓN / INSTITUTION: - Pathology, University of Alabama at Birmingham.

RESUMEN / SUMMARY: - PURPOSE: Activating extrinsic apoptotic pathways targeting death receptors (DR) using agonistic antibodies or tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) is promising for cancer therapy. However, most pancreatic cancers are resistant to TRAIL therapy. The present studies aimed to identify combination therapies that enhance the efficacy of TRAIL therapy; and to investigate the underlying mechanisms. EXPERIMENTAL DESIGN: A xenograft model in nude mice was used to determine pancreatic cancer tumorigenesis and therapeutic efficacy of TRA-8, a monoclonal agonistic antibody for DR5. Pancreatic cancer cells were used to characterize mechanisms underlying poly(ADP-ribose) polymerase-1 (PARP-1) in regulating TRA-8-induced apoptosis in vitro. RESULTS: PARP-1 was found highly expressed in the TRA-8-resistant PANC-1 and Suit-2 cells, compared with TRA-8-sensitive BxPc-3 and MiaPaca-2. Inhibition of PARP-1 with a pharmacologic inhibitor sensitized PANC-1 and Suit2 cells to TRA-8 induced apoptosis in a dose-dependent manner. Furthermore, small interfering RNAs specifically knocking down PARP-1 markedly enhanced TRA-8-induced apoptosis in vitro, and augmented the efficacy of TRA-8 therapy on tumorigenesis in vivo. PARP-1 knockdown increased TRA-8-induced activation of caspase-8 in the death-induced signaling complex (DISC). Immuoprecipitation with DR5 antibody identified the recruitment of PARP-1 and PARP-1-mediated protein poly-ADP-ribosylation(pADPr) modification in the DR5-associated DISC. Further characterization revealed that PARP-1-mediated pADPr modification of caspase-8 inhibited caspase-8 activation, which may contribute to its function in regulating TRA-8 resistance. CONCLUSIONS: Our studies provide molecular insights into a novel function of PARP-1 in regulating the extrinsic apoptosis machinery, and also support interventions combining PARP-1 inhibitors with death receptor agonists for pancreatic cancer therapy.

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[64]

TÍTULO / TITLE: - Lamin B1 Is a Novel Therapeutic Target of Betulinic Acid in Pancreatic Cancer.

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

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

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-12-3630

AUTORES / AUTHORS: - Li L; Du Y; Kong X; Li Z; Jia Z; Cui J; Gao J; Wang L; Xie K

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

RESUMEN / SUMMARY: - PURPOSE: Betulinic acid (BA), a naturally occurring pentacyclic triterpenoid, exhibits potent anti-tumor activities, whereas the underlying mechanisms remain unclear. In current study, we sought to determine the role and regulation of lamin B1 expression in human pancreatic cancer pathogenesis and BA-based therapy. EXPERIMENTAL DESIGN: We used cDNA microarray to identify BA target genes and used tissue microarray to determine the expression levels of lamin B1 in pancreatic cancer tissues and to define their relationship with the clinicopathologic characteristics of pancreatic cancer. We also used in vitro and in vivo models to determine the biological impacts of altered lamin B1 expression on and mechanisms underlying lamin B1 overexpression in human pancreatic cancer. RESULTS: We found that lamin B1 was significantly downregulated by BA treatment in pancreatic cancer in both in vitro culture and xenograft models. Overexpression of lamin B1 was pronounced in human pancreatic cancer and increased lamin B1 expression was directly associated with low grade differentiation, increased incidence of distant metastasis and poor prognosis of pancreatic cancer patients. Furthermore, knockdown of lamin B1 significantly attenuated the proliferation, invasion and tumorigenicity of pancreatic cancer cells. CONCLUSIONS: Lamin B1 plays an important role in pancreatic cancer pathogenesis and is a novel therapeutic target of BA treatment.

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[65]

TÍTULO / TITLE: - Disease Spectrum of Intraductal Papillary Mucinous Neoplasm With an Associated Invasive Carcinoma: Invasive IPMN Versus Pancreatic Ductal Adenocarcinoma-Associated IPMN.

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

REVISTA / JOURNAL: - Pancreas. 2013 Jul 16.

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

1097/MPA.0b013e3182954137

AUTORES / AUTHORS: - Kang MJ; Lee KB; Jang JY; Kwon W; Park JW; Chang YR; Kim SW

INSTITUCIÓN / INSTITUTION: - From the *Department of Surgery and Cancer Research Institute, and daggerDepartment of Pathology, Seoul National University College of Medicine, Seoul, South Korea.

RESUMEN / SUMMARY: - OBJECTIVES: Current version of World Health Organization classification introduced the concept of “intraductal papillary mucinous neoplasm (IPMN) with an associated invasive carcinoma.” The authors investigated the clinicopathologic characteristics and prognosis of this disease category according to tumor morphology and percentage of invasive component. METHODS: Fifty-nine patients who underwent surgical resection of IPMN with an associated invasive carcinoma at Seoul National University

Hospital were subgrouped according to the invasive component of less than 5% (minimally invasive [MI] intraductal papillary mucinous carcinoma [IPMC] [MI-IPMC]), 5%-50% (invasive IPMC [IPMC-I]), and 50% or greater (pancreatic ductal adenocarcinoma [PDAC]-associated IPMN [PDAC-IPMN]). Prognosis was compared with 219 curatively resected conventional PDAC. RESULTS: Eleven MI-IPMCs (18.6%), 24 IPMC-Is (40.7%), and 24 PDAC-IPMNs (40.7%) were identified. With the transition from MI-IPMC to IPMC-I and PDAC-IPMN, percentage of advanced T ($P < 0.001$) or N stage ($P = 0.001$), expression of S100A4 ($P = 0.004$), p53 ($P = 0.028$), and CD24 ($P = 0.009$) increased; and SMAD4 expression decreased ($P < 0.001$). The overall 5-year survival rates for MI-IPMC, IPMC-I, and PDAC-IPMN were 80.8%, 59.0%, and 29.3%, respectively ($P < 0.001$). Pancreatic ductal adenocarcinoma-associated IPMN had poor prognosis compared with MI-IPMC ($P = 0.011$) or IPMC-I ($P = 0.026$) but had comparable prognosis with conventional PDAC ($P = 0.138$). CONCLUSIONS: Pancreatic ductal adenocarcinoma-associated IPMN has different clinicopathological characteristics compared with the IPMC-I. Intraductal papillary mucinous neoplasm with an associated invasive carcinoma is composed of a wide spectrum of disease.

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[66]

TÍTULO / TITLE: - Pattern of breast cancer susceptibility gene 1 expression is a potential prognostic biomarker in resectable pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Pancreas. 2013 Aug;42(6):977-82. doi: 10.1097/MPA.0b013e318287885c.

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

1097/MPA.0b013e318287885c

AUTORES / AUTHORS: - Wang T; Wentz SC; Ausborn NL; Washington MK; Merchant N; Zhao Z; Shyr Y; Chakravarthy AB; Xia F

INSTITUCIÓN / INSTITUTION: - From the *Department of Radiation Oncology, daggerDepartment of Pathology, double daggerDepartment of Surgery, and section signDepartment of Biostatistics, School of Medicine,Vanderbilt University, Nashville, TN; and parallelDepartment of Radiation Oncology, College of Medicine, The Ohio State University, Columbus, OH.

RESUMEN / SUMMARY: - OBJECTIVES: The tumor-suppressor breast cancer susceptibility gene 1 (BRCA1) is a nuclear-cytoplasmic shuttling protein that when in the nucleus is required for DNA repair whereas when in the cytoplasm is important in activating cell death processes. Although BRCA1 mutations have been shown to be associated with an increased risk of pancreatic ductal adenocarcinoma (PDAC), its role in disease progression is yet to be determined. We hypothesized that BRCA1 expression pattern could be used as a prognostic biomarker. METHODS: Sixty-seven patients who underwent resections for PDAC were included. A tissue microarray was constructed,

stained with antibodies to BRCA1, and scored for intensity and subcellular location. Univariate and multivariate statistical analyses were performed. RESULTS: An increase in cytosolic BRCA1 distribution was associated with higher pathologic stage (P = 0.006). Nuclear-cytosolic BRCA1 distribution was associated with a decrease in recurrence-free survival with a hazards ratio of 1.4 (P = 0.059). Decreased BRCA1 intensity was associated with higher pathologic stage (P = 0.027), but BRCA1 intensity was not associated with overall survival or recurrence-free survival. CONCLUSIONS: Our results demonstrate a possible association of BRCA1 expression pattern with pathologic stage, implying a potential role of BRCA1 in PDAC development and progression.

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[67]

TÍTULO / TITLE: - Putting GWAS to the functional test: NR5A2 and pancreatic cancer risk.

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

REVISTA / JOURNAL: - Gut. 2013 Jun 12.

●● Enlace al texto completo (gratuito o de pago) 1136/gutjnl-2013-305030

AUTORES / AUTHORS: - Murtaugh LC

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[68]

TÍTULO / TITLE: - Measuring mitochondrial uncoupling protein-2 level and activity in insulinoma cells.

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

REVISTA / JOURNAL: - Methods Enzymol. 2013;528:257-67. doi: 10.1016/B978-0-12-405881-1.00015-X.

●● Enlace al texto completo (gratuito o de pago) 1016/B978-0-12-405881-1.00015-X

AUTORES / AUTHORS: - Barlow J; Hirschberg V; Brand MD; Affourtit C

INSTITUCIÓN / INSTITUTION: - School of Biomedical and Biological Sciences, Plymouth University, Drake Circus, Plymouth, United Kingdom.

RESUMEN / SUMMARY: - Mitochondrial uncoupling protein-2 (UCP2) regulates glucose-stimulated insulin secretion (GSIS) by pancreatic beta cells-the physiological role of the beta cell UCP2 remains a subject of debate. Experimental studies informing this debate benefit from reliable measurements of UCP2 protein level and activity. In this chapter, we describe how UCP2 protein can be detected in INS-1 insulinoma cells and how it can be knocked down by RNA interference. We demonstrate briefly that UCP2 knockdown lowers glucose-induced rises in mitochondrial respiratory activity, coupling efficiency of oxidative phosphorylation, levels of mitochondrial reactive oxygen species, and insulin secretion. We provide protocols for the detection of the

respective UCP2 phenotypes, which are indirect, but invaluable measures of UCP2 activity. We also introduce a convenient method to normalize cellular respiration to cell density allowing measurement of UCP2 effects on specific mitochondrial oxygen consumption.

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[69]

TÍTULO / TITLE: - Belinostat-induced apoptosis and growth inhibition in pancreatic cancer cells involve activation of TAK1-AMPK signaling axis.

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

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Jul 19;437(1):1-6. doi: 10.1016/j.bbrc.2013.05.090. Epub 2013 Jun 4.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bbrc.2013.05.090

AUTORES / AUTHORS: - Wang B; Wang XB; Chen LY; Huang L; Dong RZ

INSTITUCIÓN / INSTITUTION: - Department of Abdominal Surgical Oncology, Zhejiang Cancer Hospital, Hangzhou, Zhejiang 310022, China. Electronic address: wangbin69@yahoo.com.

RESUMEN / SUMMARY: - Pancreatic cancer accounts for more than 250,000 deaths worldwide each year. Recent studies have shown that belinostat, a novel pan histone deacetylases inhibitor (HDACi) induces apoptosis and growth inhibition in pancreatic cancer cells. However, the underlying mechanisms are not fully understood. In the current study, we found that AMP-activated protein kinase (AMPK) activation was required for belinostat-induced apoptosis and anti-proliferation in PANC-1 pancreatic cancer cells. A significant AMPK activation was induced by belinostat in PANC-1 cells. Inhibition of AMPK by RNAi knockdown or dominant negative (DN) mutation significantly inhibited belinostat-induced apoptosis in PANC-1 cells. Reversely, AMPK activator AICAR and A-769662 exerted strong cytotoxicity in PANC-1 cells. Belinostat promoted reactive oxygen species (ROS) production in PANC-1 cells, increased ROS induced transforming growth factor-beta-activating kinase 1 (TAK1)/AMPK association to activate AMPK. Meanwhile, anti-oxidants N-Acetyl-Cysteine (NAC) and MnTBAP as well as TAK1 shRNA knockdown suppressed belinostat-induced AMPK activation and PANC-1 cell apoptosis. In conclusion, we propose that belinostat-induced apoptosis and growth inhibition require the activation of ROS-TAK1-AMPK signaling axis in cultured pancreatic cancer cells.

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[70]

TÍTULO / TITLE: - Role of the eIF4E binding protein 4E-BP1 in regulation of the sensitivity of human pancreatic cancer cells to TRAIL and celastrol-induced apoptosis.

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

REVISTA / JOURNAL: - Biol Cell. 2013 Jun 4. doi: 10.1111/boc.201300021.

●● Enlace al texto completo (gratuito o de pago) 1111/boc.201300021

AUTORES / AUTHORS: - Chakravarthy R; Clemens MJ; Pirianov G; Perdios N; Mudan S; Cartwright JE; Elia A

INSTITUCIÓN / INSTITUTION: - Translational Control Group, Division of Biomedical Sciences, St George's, University of London, London, SW17 0RE, UK.

RESUMEN / SUMMARY: - BACKGROUND INFORMATION: Tumour cells can be induced to undergo apoptosis after treatment with the tumour necrosis factor alpha-related death-inducing ligand (TRAIL). Although human pancreatic cancer cells show varying degrees of response they can be sensitised to the pro-apoptotic effects of TRAIL in the presence of celastrol, a natural compound extracted from the plant Tripterygium wilfordii Hook F. One important aspect of the cellular response to TRAIL is the control of protein synthesis, a key regulator of which is the eukaryotic initiation factor 4E-binding protein, 4E-BP1. RESULTS: We examined the effects of celastrol and TRAIL in several pancreatic cancer cell lines. In cells that are normally resistant to TRAIL, synergistic effects of TRAIL plus celastrol on commitment to apoptosis and inhibition of protein synthesis were observed. These were associated with a strong up-regulation and dephosphorylation of 4E-BP1. The enhancement of 4E-BP1 expression, which correlated with a threefold increase in the level of the 4E-BP1 transcript, was blocked by inhibitors of reactive oxygen species and the JNK protein kinase. When the expression of 4E-BP1 was reduced by an inducible micro-RNA, TRAIL-mediated apoptosis was inhibited. CONCLUSION: These results suggest that 4E-BP1 plays a critical role in the mechanism by which TRAIL and celastrol together cause apoptotic cell death in human pancreatic tumour cells.

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[71]

TÍTULO / TITLE: - Potential predictors of disease progression for main-duct intraductal papillary mucinous neoplasms of the pancreas.

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

REVISTA / JOURNAL: - J Gastroenterol Hepatol. 2013 Jun 25. doi: 10.1111/jgh.12301.

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

AUTORES / AUTHORS: - Ogura T; Masuda D; Kurisu Y; Edogawa S; Imoto A; Hayashi M; Uchiyama K; Higuchi K

INSTITUCIÓN / INSTITUTION: - Second Department of Internal Medicine, Osaka Medical College, Osaka, Japan.

RESUMEN / SUMMARY: - BACKGROUND AND AIM: The evidence for main-duct intraductal papillary mucinous neoplasms (MPD-IPMN) malignancy is based predominantly on investigation of resected cases and the natural history is still unclear. The aim of the present study is to investigate the natural history of MPD-IPMN and examine potential predictors of disease progression in MPD-IPMN patients who conformed to 'high-risk stigmata' criteria. METHODS: This

study included consecutive follow up 20 patients and surgical patients with 'high-risk stigmata' MPD-IPMN, in whom the diameter of the MPD was >10 mm, branch duct was <5 mm, and who underwent clinical follow-up for >/=2 years. RESULTS: Among surgical patients, mural nodules and MPD diameter of invasive patients were significantly differences compared with non-invasive patients. On the other hand, among follow up patients, univariate analysis revealed the following potential predictors for disease progression: diameter of MPD >/=15 mm (hazard ratio (HR), 20.9; 95% confidence interval (CI), 2.59-173.4 P<0.01); and diffuse lesions of MPD-IPMN (HR, 4.46; 95%CI, 1.10-18.0; P=0.04). On the other hand, multivariate analysis identified only diameter of MPD >/=15 mm (HR, 19.2; 95%CI, 1.87-198.5; P=0.01) as a potential predictor of disease progression. CONCLUSION: If MPD-IPMN patients have other severe complications or reasons for not undergoing surgical treatment, MPD diameter <15 mm, negative cytology, and no mural nodules, conservative clinical follow-up for several years may be an option.

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[72]

TÍTULO / TITLE: - Differential Expression of Cytochrome P450 Omega-hydroxylase Isoforms and Their Association with Clinicopathological Features in Pancreatic Ductal Adenocarcinoma.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Jul 12.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3128-x

AUTORES / AUTHORS: - Gandhi AV; Saxena S; Relles D; Sarosiek K; Kang CY; Chipitsyna G; Andrel Sendecki J; Yeo CJ; Arafat HA

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Jefferson Pancreatic Biliary and Related Cancer Center, Thomas Jefferson University Hospital, Thomas Jefferson University, Philadelphia, PA, USA.

RESUMEN / SUMMARY: - BACKGROUND: The cytochrome P450 (CYP) superfamily consists of enzymes that catalyze the oxidation of lipids, steroids, and drugs. In particular, the CYP4 family plays an essential role in lipid metabolism by the omega-hydroxylation of terminal ends of fatty acids. Disturbance of this system has been associated with increased angiogenesis, proliferation, and metastasis of several cancers. This study aimed to detect the expression of CYP4 isoforms (CYP4A11, CYP4F2, CYP4F3) in pancreatic ductal adenocarcinoma (PDA) and their association with clinicopathological features. METHODS: Pancreatic specimens were collected from 73 patients who underwent surgical resection at the Thomas Jefferson University Hospital. Quantitative polymerase chain reaction was used to examine the cytochrome P450 isoforms in PDA (n = 62), adjacent-normal (n = 30), and benign tissues (n = 11). Logistic regression models were used to analyze gene expression among tissue types. Spearman rank correlations were calculated for isoform

expression and for age. Differences in expression by gender were assessed via t test. Other clinicopathological variables (diabetes, smoking, obesity, T stage, perineural invasion, nodal status) were analyzed by Wilcoxon rank sum. RESULTS: CYP4 expression for isoforms was significantly higher in PDA tissues versus matched-adjacent tissues ($p < 0.01$). PDA tumors expressed significantly higher levels of CYP4F2 and CYP4F3 when compared to benign lesions ($p < 0.01$). Significant associations were found between low levels of CYP4F2 and CYP4F3 and increased age of PDA patients. Interestingly, all isoforms were expressed at higher levels in male patients. CONCLUSIONS: Transcriptional upregulation of cytochrome P450 omega-hydroxylase suggests that these enzymes have the potential to be used as distinguishing markers in pancreatic pathology.

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[73]

TÍTULO / TITLE: - Inhibition of Protein Phosphatase 2ª Radiosensitizes Pancreatic Cancers by Modulating CDC25C/CDK1 and Homologous Recombination Repair.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Jul 19.

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-0788

AUTORES / AUTHORS: - Wei D; Parsels LA; Karnak D; Davis MA; Parsels JD; Marsh AC; Zhao L; Maybaum J; Lawrence TS; Sun Y; Morgan MA

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of Radiation Oncology and Pharmacology, University of Michigan Medical School, and Department of Biostatistics, University of Michigan Comprehensive Cancer Center, Ann Arbor, Michigan.

RESUMEN / SUMMARY: - PURPOSE: To identify targets whose inhibition may enhance the efficacy of chemoradiation in pancreatic cancer and thus improve survival, we conducted an siRNA library screen in pancreatic cancer cells. We investigated PPP2R1A, a scaffolding subunit of protein phosphatase 2ª (PP2A) as a lead radiosensitizing target.EXPERIMENTAL DESIGN: We determined the effect of PP2A inhibition by genetic (PPP2R1A siRNA) and pharmacologic (LB100, a small molecule entering phase I clinical trials) approaches on radiosensitization of Panc-1 and MiaPaCa-2 pancreatic cancer cells both in vitro and in vivo.RESULTS: PPP2R1A depletion by siRNA radiosensitized Panc-1 and MiaPaCa-2 cells, with radiation enhancement ratios of 1.4 ($P < 0.05$). Likewise, LB100 produced similar radiosensitization in pancreatic cancer cells, but minimal radiosensitization in normal small intestinal cells. Mechanistically, PPP2R1A siRNA or LB100 caused aberrant CDK1 activation, likely resulting from accumulation of the active forms of PLK1 (pPLK1 T210) and CDC25C (pCDC25C T130). Furthermore, LB100 inhibited radiation-induced Rad51 focus formation and homologous recombination repair (HRR), ultimately leading to

persistent radiation-induced DNA damage, as reflected by gamma-H2AX expression. Finally, we identified CDC25C as a key PP2A substrate involved in LB100-mediated radiosensitization as depletion of CDC25C partially reversed LB100-mediated radiosensitization. In a mouse xenograft model of human pancreatic cancer, LB100 produced significant radiosensitization with minimal weight loss.CONCLUSIONS: Collectively, our data show that PP2A inhibition radiosensitizes pancreatic cancer both in vitro and in vivo via activation of CDC25C/CDK1 and inhibition of HRR, and provide proof-of-concept evidence that PP2A is a promising target for the improvement of local therapy in pancreatic cancer. Clin Cancer Res; 1-11. ©2013 AACR.

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[74]

TÍTULO / TITLE: - Integration of KRAS testing in the diagnosis of pancreatic cystic lesions: a clinical experience of 618 pancreatic cysts.

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

REVISTA / JOURNAL: - Mod Pathol. 2013 Jun 7. doi: 10.1038/modpathol.2013.91.

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

1038/modpathol.2013.91

AUTORES / AUTHORS: - Nikiforova MN; Khalid A; Fasanella KE; McGrath KM; Brand RE; Chennat JS; Slivka A; Zeh HJ; Zureikat AH; Krasinskas AM; Ohori NP; Schoedel KE; Navina S; Mantha GS; Pai RK; Singhi AD

INSTITUCIÓN / INSTITUTION: - Department of Pathology, The University of Pittsburgh Medical Center, Pittsburgh, PA, USA.

RESUMEN / SUMMARY: - With improvements in abdominal imaging, detection of incidental pancreatic cysts are becoming increasingly common. Analysis of pancreatic cyst fluid from fine-needle aspiration is particularly important in identifying intraductal papillary mucinous neoplasms (IPMNs) and mucinous cystic neoplasms (MCNs), which have significant implications in clinical intervention and follow-up. Previous controlled studies have shown that KRAS mutations in cyst fluid are highly specific for mucinous differentiation in pancreatic cysts; however, this has not been examined in the clinical setting. Over a 6-year study period, 618 pancreatic cyst fluids obtained by fine-needle aspiration at the time of endoscopic ultrasound were tested for KRAS mutations as part of routine evaluation for a cystic neoplasm. Of the 618 specimens, 603 (98%) from 546 patients were satisfactory for molecular analysis. Patients ranged in age from 17 to 90 years (mean, 63.9 years) and were predominantly female (68%). Pancreatic cysts were relatively evenly distributed throughout the pancreas and ranged in size from 0.6 to 11.0 cm (mean, 2.3 cm). Mutations in KRAS were detected in 232 of 603 (38%) aspirates. Although sufficient for molecular analysis, 320 of 603 (53%) specimens were either less than optimal (38%) or unsatisfactory (15%) for cytopathologic diagnosis. Surgical follow-up information was available for 142 (26%) patients and consisted of 53 KRAS-

mutated and 89 KRAS-wild-type cysts. Overall, KRAS mutations had a specificity of 100%, but a sensitivity of 54% for mucinous differentiation. When stratified by cyst type, KRAS had a sensitivity of 67% and 14% for IPMNs and MCNs, respectively. In summary, KRAS mutations were highly specific for mucinous differentiation, but were inadequate in identifying MCNs. Future molecular studies and the combination of other fluid markers are required to improve the detection and classification of pancreatic mucinous neoplasms by endoscopic ultrasound fine-needle aspiration.Modern Pathology advance online publication, 7 June 2013; doi:10.1038/modpathol.2013.91.

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[75]

TÍTULO / TITLE: - One year of sitagliptin treatment protects against islet amyloid-associated beta-cell loss and does not induce pancreatitis or pancreatic neoplasia in mice.

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

REVISTA / JOURNAL: - Am J Physiol Endocrinol Metab. 2013 Jun 4.

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

1152/ajpendo.00025.2013

AUTORES / AUTHORS: - Aston-Mourney K; Subramanian SL; Zraika S; Samarasekera T; Meier DT; Goldstein LC; Hull RL

INSTITUCIÓN / INSTITUTION: - 1VA Puget Sound Health Care Sytem and University of Washington.

RESUMEN / SUMMARY: - The DPP-4 inhibitor sitagliptin is an attractive therapy for diabetes as it increases insulin release and may preserve beta-cell mass. However, sitagliptin also increases beta-cell release of human islet amyloid polypeptide (hIAPP), the peptide component of islet amyloid, which is co-secreted with insulin. Thus, sitagliptin treatment may promote islet amyloid formation and its associated beta-cell toxicity. Conversely, metformin treatment decreases islet amyloid formation by decreasing beta-cell secretory demand, and could therefore offset sitagliptin's potential pro-amyloidogenic effects. Sitagliptin treatment has also been reported to be detrimental to the exocrine pancreas. We investigated whether long-term sitagliptin treatment, alone or with metformin, increased islet amyloid deposition and beta-cell toxicity, and induced pancreatic ductal proliferation, pancreatitis and/or pancreatic metaplasia/neoplasia. hIAPP transgenic and non-transgenic littermates were followed for one year on no treatment, sitagliptin, metformin, or the combination. Islet amyloid deposition, beta-cell mass, insulin release and measures of exocrine pancreas pathology were determined. Relative to untreated mice, sitagliptin treatment did not increase amyloid deposition, despite increasing hIAPP release, and prevented amyloid-induced beta-cell loss. Metformin treatment alone or with sitagliptin decreased islet amyloid deposition to a similar extent vs untreated mice. Ductal proliferation was not altered among treatment groups and no evidence of pancreatitis, ductal metaplasia or neoplasia, were

observed. Therefore, long-term sitagliptin treatment stimulates beta-cell secretion without increasing amyloid formation and protects against amyloid-induced beta-cell loss. This suggests a novel effect of sitagliptin to protect the beta cell in type 2 diabetes which appears to occur without adverse effects on the exocrine pancreas.

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[76]

TÍTULO / TITLE: - Cisplatin-induced non-apoptotic death of pancreatic cancer cells requires mitochondrial cyclophilin-D-p53 signaling.

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

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Jul 8. pii: S0006-291X(13)01113-3. doi: 10.1016/j.bbrc.2013.06.103.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bbrc.2013.06.103

AUTORES / AUTHORS: - Chen B; Xu M; Zhang H; Wang JX; Zheng P; Gong L; Wu GJ; Dai T

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, East Hospital Affiliated to Tongji University in Shanghai, Shanghai, China.

RESUMEN / SUMMARY: - The pancreatic cancer remains a fatal disease for the majority of patients. Cisplatin has displayed significant cytotoxic effects against the pancreatic cancer cells, however the underlying mechanisms remain inconclusive. Here, we found that cisplatin mainly induced non-apoptotic death of the pancreatic cancer cells (AsPC-1 and Capan-2), which was associated with a significant p53 activation (phosphorylation and accumulation). Further, activated p53 was found to translocate to mitochondria where it formed a complex with cyclophilin D (Cyp-D). We provided evidences to support that mitochondrial Cyp-D/p53 complexation might be critical for cisplatin-induced non-apoptotic death of pancreatic cancer cells. Inhibition of Cyp-D by its inhibitor cyclosporine A (CsA), or by shRNA-mediated knockdown suppressed cisplatin-induced pancreatic cancer cell death. Both CsA and Cyp-D knockdown also disrupted the Cyp-D/p53 complex formation in mitochondria. Meanwhile, the pancreatic cancer cells with p53 knockdown were resistant to cisplatin. On the other hand, HEK-293 over-expressing Cyp-D were hyper-sensitive to cisplatin. Interestingly, camptothecin (CMT)-induced pancreatic cancer cell apoptotic death was not affected CsA or Cyp-D knockdown. Together, these data suggested that cisplatin-induced non-apoptotic death requires mitochondria Cyp-D-p53 signaling in pancreatic cancer cells.

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[77]

TÍTULO / TITLE: - Interactions between dietary flavonoids apigenin or luteolin and chemotherapeutic drugs to potentiate anti-proliferative effect on human pancreatic cancer cells, in vitro.

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

REVISTA / JOURNAL: - Food Chem Toxicol. 2013 Jul 18. pii: S0278-6915(13)00491-2. doi: 10.1016/j.fct.2013.07.036.

●● Enlace al texto completo (gratuito o de pago) 1016/j.fct.2013.07.036

AUTORES / AUTHORS: - Johnson JL; Gonzalez de Mejia E

INSTITUCIÓN / INSTITUTION: - Division of Nutritional Sciences, University of Illinois at Urbana-Champaign, 228 ERML, 1201 W Gregory Drive, Urbana, IL 61801, USA.

RESUMEN / SUMMARY: - The objectives were to assess the potential of dietary flavonoids apigenin (Api) and luteolin (Lut) to enhance the anti-proliferative effects of chemotherapeutic drugs on BxPC-3 human pancreatic cancer cells and to investigate the potential molecular mechanism of action. Simultaneous treatment or pretreatment (0, 6, 24 and 42h) of flavonoids and chemotherapeutic drugs and various concentrations (0-50muM) were assessed using the MTS cell proliferation assay. Simultaneous treatment with either flavonoid (0,13, 25 or 50muM) and chemotherapeutic drugs 5-fluorouracil (5-FU, 50muM) or gemcitabine (Gem, 10muM) for 60h resulted in less-than-additive effect ($p<0.05$). Pretreatment for 24h with 13muM of either Api or Lut, followed by Gem for 36h was optimal to inhibit cell proliferation. Pretreatment of cells with 11-19muM of either flavonoid for 24h resulted in 59-73% growth inhibition when followed by Gem (10muM, 36h). Lut (15muM, 24h) pretreatment followed by Gem (10muM, 36h), significantly decreased protein expression of nuclear GSK-3beta and NF-kappaB p65 and increased pro-apoptotic cytosolic cytochrome c. Pretreatment of human pancreatic cancer cells BxPC-3 with low concentrations of Api or Lut effectively aid in the anti-proliferative activity of chemotherapeutic drugs.

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[78]

TÍTULO / TITLE: - Dietary intake of acrylamide and pancreatic cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort.

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

REVISTA / JOURNAL: - Ann Oncol. 2013 Jul 14.

●● Enlace al texto completo (gratuito o de pago) 1093/annonc/mdt255

AUTORES / AUTHORS: - Obon-Santacana M; Slimani N; Lujan-Barroso L; Travier N; Hallmans G; Freisling H; Ferrari P; Boutron-Ruault MC; Racine A; Clavel F; Saieva C; Pala V; Tumino R; Mattiello A; Vineis P; Arguelles M; Ardanaz E; Amiano P; Navarro C; Sanchez MJ; Molina Montes E; Key T; Khaw KT; Wareham N; Peeters PH; Trichopoulou A; Bamia C; Trichopoulos D; Boeing H; Kaaks R; Katzke V; Ye W; Sund M; Ericson U; Wirfalt E; Overvad K; Tjonneland A; Olsen A; Skeie G; Asli LA; Weiderpass E; Riboli E; Bueno-de-Mesquita HB; Duell EJ

INSTITUCIÓN / INSTITUTION: - Unit of Nutrition, Environment and Cancer, Cancer Epidemiology Research Program, Catalan Institute of Oncology (ICO-IDIBELL), Barcelona, España.

RESUMEN / SUMMARY: - BACKGROUND: In 1994, acrylamide (AA) was classified as a probable human carcinogen by the International Agency for Research on Cancer. In 2002, AA was discovered at relatively high concentrations in some starchy, plant-based foods cooked at high temperatures. PATIENTS AND METHODS: A prospective analysis was conducted to evaluate the association between the dietary intake of AA and ductal adenocarcinoma of the exocrine pancreatic cancer (PC) risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort using Cox regression modeling. EPIC includes >500 000 men and women aged 35-75 at enrollment from 10 European countries. AA intake was estimated for each participant by combining questionnaire-based food consumption data with a harmonized AA database derived from the EU monitoring database of AA levels in foods, and evaluated in quintiles and continuously. RESULTS: After a mean follow-up of 11 years, 865 first incident adenocarcinomas of the exocrine pancreas were observed and included in the present analysis. At baseline, the mean dietary AA intake in EPIC was 26.22 microg/day. No overall association was found between continuous or quintiles of dietary AA intake and PC risk in EPIC (HR:0.95, 95%CI:0.89-1.01 per 10 microg/day). There was no effect measure modification by smoking status, sex, diabetes, alcohol intake or geographic region. However, there was an inverse association (HR: 0.73, 95% CI: 0.61-0.88 per 10 microg/day) between AA intake and PC risk in obese persons as defined using the body mass index (BMI, >/=30 kg/m2), but not when body fatness was defined using waist and hip circumference or their ratio. CONCLUSIONS: Dietary intake of AA was not associated with an increased risk of PC in the EPIC cohort.

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[79]

TÍTULO / TITLE: - Pharmacodynamic modeling of cell cycle and apoptotic effects of gemcitabine on pancreatic adenocarcinoma cells.

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

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Jul 9.

●● Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2226-6

AUTORES / AUTHORS: - Hamed SS; Straubinger RM; Jusko WJ

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical Sciences, School of Pharmacy and Pharmaceutical Sciences, University at Buffalo, 404 Kapoor Hall, Buffalo, NY, 14214, USA.

RESUMEN / SUMMARY: - PURPOSE: The standard of care for treating patients with pancreatic adenocarcinomas includes gemcitabine (2',2'-difluorodeoxycytidine). Gemcitabine primarily elicits its response by stalling the DNA replication forks of cells in the S phase of the cell cycle. To provide a quantitative framework for characterizing the cell cycle and apoptotic effects of gemcitabine, we developed a pharmacodynamic model in which the activation

of cell cycle checkpoints or cell death is dependent on gemcitabine exposure. METHODS: Three pancreatic adenocarcinoma cell lines (AsPC-1, BxPC-3, and MiaPaca-2) were exposed to varying concentrations (0-100,000 ng/mL) of gemcitabine over a period of 96 h in order to quantify proliferation kinetics and cell distributions among the cell cycle phases. The model assumes that the drug can inhibit cycle-phase transitioning in each of the 3 phases (G1, S, and G2/M) and can cause apoptosis of cells in G1 and G2/M phases. Fitting was performed using the ADAPT5 program. RESULTS: The time course of gemcitabine effects was well described by the model, and parameters were estimated with good precision. Model predictions and experimental data show that gemcitabine induces cell cycle arrest in the S phase at low concentrations, whereas higher concentrations induce arrest in all cell cycle phases. Furthermore, apoptotic effects of gemcitabine appear to be minimal and take place at later time points. CONCLUSION: The pharmacodynamic model developed provides a quantitative, mechanistic interpretation of gemcitabine efficacy in 3 pancreatic cancer cell lines, and provides useful insights for rational selection of chemotherapeutic agents for combination therapy.

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[80]

TÍTULO / TITLE: - Clinicopathological Correlates of Activating GNAS Mutations in Intraductal Papillary Mucinous Neoplasm (IPMN) of the Pancreas.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Jul 12.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3096-1

AUTORES / AUTHORS: - Dal Molin M; Matthaei H; Wu J; Blackford A; Debeljak M; Rezaee N; Wolfgang CL; Butturini G; Salvia R; Bassi C; Goggins MG; Kinzler KW; Vogelstein B; Eshleman JR; Hruban RH; Maitra A

INSTITUCIÓN / INSTITUTION: - Department of Pathology, The Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA.

RESUMEN / SUMMARY: - BACKGROUND: Intraductal papillary mucinous neoplasms (IPMNs) are the most common cystic precursor lesions of invasive pancreatic cancer. The recent identification of activating GNAS mutations at codon 201 in IPMNs is a promising target for early detection and therapy. The purpose of this study was to explore clinicopathological correlates of GNAS mutational status in resected IPMNs. METHODS: Clinical and pathologic characteristics were retrieved on 54 patients in whom GNAS codon 201 mutational status was previously reported (“historical group”, Wu et al. Sci Transl Med 3:92ra66, 2011). In addition, a separate cohort of 32 patients (validation group) was included. After microdissection and DNA extraction, GNAS status was determined in the validation group by pyrosequencing. RESULTS: GNAS activating mutations were found in 64 % of the 32 IPMNs

included in the validation group, compared with a previously reported prevalence of 57 % in the historical group. Overall, 52 of 86 (61 %) of IPMNs demonstrated GNAS mutations in the two studies combined. Analysis of both groups confirmed that demographic characteristics, tumor location, ductal system involvement, focality, size, grade of dysplasia, presence of an associated cancer, and overall survival were not correlated with GNAS mutational status. Stratified by histological subtype, 100 % of intestinal type IPMNs demonstrated GNAS mutations compared to 51 % of gastric IPMN, 71 % of pancreatobiliary IPMNs, and 0 % of oncocytic IPMNs. CONCLUSIONS: GNAS activating mutations can be reliably detected in IPMNs by pyrosequencing. In terms of clinicopathological parameters, only histological subtype was correlated with mutational frequency, with the intestinal phenotype always associated with GNAS mutations.

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[81]

TÍTULO / TITLE: - En bloc pancreaticoduodenectomy and right colectomy in the treatment of locally advanced colon cancer.

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

REVISTA / JOURNAL: - Dis Colon Rectum. 2013 Jul;56(7):874-80. doi: 10.1097/DCR.0b013e3182941704.

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

1097/DCR.0b013e3182941704

AUTORES / AUTHORS: - Zhang J; Leng JH; Qian HG; Qiu H; Wu JH; Liu BN; Li CP; Hao CY

INSTITUCIÓN / INSTITUTION: - Key Laboratory of Carcinogenesis and Translational Research, Ministry of Education, Department of Hepato-Pancreatic Biliary Surgery, Beijing Cancer Hospital, Peking University Cancer Hospital & Institute, Beijing, China.

RESUMEN / SUMMARY: - BACKGROUD: Carcinoma of the right colon invading the pancreas or duodenum is rare. Evidence of the indication, operative morbidity, and survival of en bloc pancreaticoduodenectomy and right colectomy for right colon cancer invading adjacent organs is limited. OBJECTIVE: : The goal of this study was to investigate the feasibility, safety, indication, and long-term results of en bloc pancreaticoduodenectomy and right colectomy in the treatment of locally advanced right-sided colon cancer. DESIGN: : This was a retrospective analysis of all inpatients undergoing en bloc pancreaticoduodenectomy and right colectomy. Detailed data of these patients were assessed by a thorough review of medical charts. SETTINGS: The study was conducted using a hospital database. PATIENTS: Fourteen patients who underwent en bloc pancreaticoduodenectomy and right colectomy from January 1989 through December 2011 were included in the study. MAIN OUTCOME MEASURES: In-hospital complications, mortality, and survival were the primary outcomes measured. RESULTS: Major postoperative complications included

delayed gastric empting (n = 7), class B pancreatic fistula (n = 3), and bile leakage (n = 1). Postoperative death occurred in 2 patients. The median hospital stay was 22.5 days (range, 17.0-57.0 days). Inflammatory adhesion was confirmed by pathologic examination in only 1 patient. Eight patients (57%) did not have lymph node metastasis. The median follow-up time was 21 months (range, 4-276 months). Ten patients were alive at the time of their last scheduled follow-up. The overall survival rates were 72% at 1 year and 60% at 2 years. No patient was lost to follow-up. Three patients developed tumor recurrence. The outcomes are no worse than those of the stage-matched patients without adjacent organ involvement and are much better than those of the stage-matched patients who underwent bypass surgery and chemotherapy. LIMITATIONS: The number of patients in current studies is limited. CONCLUSIONS: En bloc pancreaticoduodenectomy and right colectomy can be performed safely with an acceptable morbidity and mortality rate in selected patients with locally advanced right-side colon cancer. The long-term results are promising.

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[82]

TÍTULO / TITLE: - Adjuvant therapy for resectable pancreatic adenocarcinoma: Review of the current treatment approaches and future directions.

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

REVISTA / JOURNAL: - Cancer Treat Rev. 2013 Jun 26. pii: S0305-7372(13)00122-9. doi: 10.1016/j.ctrv.2013.05.008.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ctrv.2013.05.008

AUTORES / AUTHORS: - Antoniou G; Kountourakis P; Papadimitriou K; Vassiliou V; Papamichael D

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, B.O.C. Oncology Centre, Nicosia, Cyprus.

RESUMEN / SUMMARY: - Adenocarcinoma of the pancreas carries a uniformly poor prognosis with high rates of loco-regional as well as systemic recurrence. Outcomes remain poor, even for early stage and resectable disease. It is perceived as inherently resistant to most of the currently available treatment options. Evidence supports the need for adjuvant chemotherapy but controversy remains in relation to the use of combined therapy, novel agents and the most appropriate timing of therapy. Despite no clear consensus, mainstay of treatment following resection is based primarily on single agent gemcitabine. Promising new agents and molecules of prognostic as well as predictive value under evaluation offer intriguing data, despite issues surrounding adjuvant therapy strategies. In this article, we sought to review the different therapeutic adjuvant modalities and future directions.

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[83]

TÍTULO / TITLE: - ONCOLYTIC VESICULAR STOMATITIS VIRUS IN IMMUNOCOMPETENT MODEL OF MUC1 POSITIVE AND MUC1 NULL PANCREATIC DUCTAL ADENOCARCINOMA.

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

REVISTA / JOURNAL: - J Virol. 2013 Jul 17.

●● Enlace al texto completo (gratuito o de pago) 1128/JVI.01412-13

AUTORES / AUTHORS: - Hastie E; Besmer DM; Shah NR; Murphy AM; Moerdyk-Schauwecker M; Molestina C; Das Roy L; Curry JM; Mukherjee P; Grdzelishvili VZ

INSTITUCIÓN / INSTITUTION: - Department of Biology, University of North Carolina at Charlotte, Charlotte, North Carolina 28223.

RESUMEN / SUMMARY: - Vesicular stomatitis virus (VSV) is a promising oncolytic agent against various malignancies. Here, for the first time, we tested VSV in vitro and in vivo in a clinically relevant, immunocompetent mouse model of pancreatic ductal adenocarcinoma (PDA). Our system allows the study of virotherapy against PDA in the context of overexpression (80% PDA patients) or no expression of human mucin 1 (MUC1), a major marker for poor prognosis in patients. In vitro, we tested three VSV recombinants, wild-type VSV, VSV-GFP, and a safe oncolytic VSV-DeltaM51-GFP, against five mouse PDA cell lines either expressing human MUC1 or MUC1-null. All viruses demonstrated significant oncolytic abilities independent of MUC1 expression, although VSV-DeltaM51-GFP was somewhat less effective in two PDA cell lines. In vivo administration of VSV-DeltaM51-GFP resulted in significant reduction of tumor growth for tested mouse PDA xenografts (+MUC1 or MUC1-null), and antitumor efficacy was further improved when the virus was combined with the chemotherapeutic drug gemcitabine. The antitumor effect was transient in all tested groups. The developed system can be used to study therapies involving various OVs and chemotherapeutics, with the goal of inducing tumor-specific immunity while preventing premature virus clearance.

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[84]

TÍTULO / TITLE: - Cavin-1 is essential for the tumor-promoting effect of caveolin-1 and enhances its prognostic potency in pancreatic cancer.

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

REVISTA / JOURNAL: - Oncogene. 2013 Jun 17. doi: 10.1038/onc.2013.223.

●● Enlace al texto completo (gratuito o de pago) 1038/onc.2013.223

AUTORES / AUTHORS: - Liu L; Xu HX; Wang WQ; Wu CT; Chen T; Qin Y; Liu C; Xu J; Long J; Zhang B; Xu YF; Ni QX; Li M; Yu XJ

INSTITUCIÓN / INSTITUTION: - Pancreatic Cancer Institute, Fudan University; Department of Pancreatic and Hepatobiliary Surgery, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China.

RESUMEN / SUMMARY: - Caveolin-1 exhibits a stage-dependent, functional fluctuation during pancreatic cancer development, but the underlying mechanisms remain unclear. Here, we report that cavin-1, a structural protein of caveolae, modulates the oncogenic function of caveolin-1 and cooperates with caveolin-1 to enhance pancreatic cancer aggressiveness. Cavin-1 expression is associated with caveolin-1 in pancreatic cancer tissue samples and cell lines, and predicts the metastatic potential of pancreatic cancer. Interactome analyses further revealed the physical interaction of cavin-1 and caveolin-1 and their colocalization in pancreatic cancer cells. Cavin-1 stabilizes caveolin-1 expression or activity by inhibiting its internalization and subsequent lysosomal degradation. More in-depth functional experiments showed that caveolin-1-enhanced aggressiveness of pancreatic cancer cells is dependent on the presence of cavin-1. In contrast, cavin-1 depletion inhibited the invasion and metastasis of pancreatic cancer cells, which could not be restored by caveolin-1-rescue construct. Tissue microarray analyses in two independent clinic cohorts also supported the augment of cavin-1 on the prognostic potency of caveolin-1, and showed that combination of cavin-1 with caveolin-1 predicted worse survival in pancreatic cancer patients. Of note, the phenotypes because of cavin-1 could not be achieved by other cavins such as cavin-2, and the tumor-promoting role of cavin-1 in pancreatic cancer was found to be largely dependent on caveolin-1 expression, which highlights the critical role of cavin-1/caveoin-1 in pancreatic cancer progression, and suggests that the interruption of cavin-1/caveolin-1 interaction is a promising therapeutic strategy for pancreatic cancer.Oncogene advance online publication, 17 June 2013; doi:10.1038/onc.2013.223.

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[85]

TÍTULO / TITLE: - Dosimetric and clinical predictors of toxicity following combined chemotherapy and moderately hypofractionated rotational radiotherapy of locally advanced pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Radiother Oncol. 2013 May 30. pii: S0167-8140(13)00224-7. doi: 10.1016/j.radonc.2013.05.011.

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

1016/j.radonc.2013.05.011

AUTORES / AUTHORS: - Cattaneo GM; Passoni P; Longobardi B; Slim N; Reni M; Cereda S; di Muzio N; Calandrino R

INSTITUCIÓN / INSTITUTION: - Medical Physics Department, San Raffaele Scientific Institute, Milan, Italy. Electronic address: cattaneo.mauro@hsr.it.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: Hypofractionated radiotherapy (RT) of pancreatic adenocarcinoma is limited by the tolerance of adjacent normal tissues. A better understanding of the influence of dosimetric variables on the rate of toxicity after RT must be considered an important goal.

METHODS AND MATERIALS: Sixty-one patients with histologically proven locally advanced disease (LAPD) were analyzed. The therapeutic strategy consisted of induction chemotherapy (ChT) followed by concurrent chemoradiotherapy (CRT). In 39 out of 61 patients the target volume was based on a four-dimensional CT (4D-CT) procedure. Delivered dose was 44.25Gy in 15 fractions to PTV2, which consisted of pancreatic tumor and regional lymph nodes considered radiologically involved; 23 out of 61 patients received a simultaneous integrated boost (SIB) to a tumor sub-volume infiltrating the great abdominal vessels (PTV1) with dose in the range of 48-58Gy. RT was delivered with Helical Tomotherapy. Dose-volume histograms (DVHs) of target volumes and organs at risk (OARs) were collected for analysis. The predictive value of clinical/dosimetric parameters was tested by univariate/multivariate analyses. RESULTS: The crude incidence of acute gastrointestinal (GI) grade 2 toxicity was 33%. The 12-month actuarial rate of “anatomical” (gastro-duodenal mucosa damage) toxicity was 13% (95% CI: 4-22%). On univariate analysis, several stomach and duodenum DVH endpoints are predictive of toxicity after moderately hypofractionated radiotherapy. Multivariate analysis confirmed that baseline performance status and the stomach V20[%] were strong independent predictors of acute GI grade 2 toxicity. The high-dose region of duodenum DVH (V45[%]; V40[%]) was strongly correlated with grade 2 “anatomical” toxicity; the best V40[%] and V45[%] cut-off values were 16% and 2.6% respectively. CONCLUSION: Regarding dosimetric indices, stomach V20[%] correlates with a higher rate of acute toxicity; more severe acute and late anatomical toxicities are related to the high dose region of duodenum DVH.

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[86]

TÍTULO / TITLE: - Risk of gastric or peritoneal recurrence, and long-term outcomes, following pancreatic cancer resection with preoperative endosonographically guided fine needle aspiration.

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

REVISTA / JOURNAL: - Endoscopy. 2013 Aug;45(8):619-26. doi: 10.1055/s-0033-1344216. Epub 2013 Jul 23.

●● Enlace al texto completo (gratuito o de pago) 1055/s-0033-1344216

AUTORES / AUTHORS: - Ngamruengphong S; Xu C; Woodward TA; Raimondo M; Stauffer JA; Asbun HJ; Wallace MB

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology and Hepatology, Mayo Clinic Florida, Jacksonville, Florida, USA.

RESUMEN / SUMMARY: - Background and study aims: There have been concerns regarding tumor cell seeding along the needle track or within the peritoneum caused by preoperative endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). The aim of this study was to evaluate whether preoperative EUS-FNA is associated with increased risk of stomach/peritoneal recurrence and whether the procedure affects long term survival.Methods: The records of

patients diagnosed with malignant solid and cystic pancreatic neoplasms who underwent surgery with curative intent between 1996 and 2012 were reviewed.Results: A total of 256 patients with similar baseline characteristics were included: 48 patients in the non-EUS-FNA group and 208 in the EUS-FNA group. Recurrence data were available for 207 patients. Median length of follow-up was 23 months (range 0 - 111 months). A total of 19 patients had gastric or peritoneal recurrence; 6 (15.4 %) in the non-EUS-FNA group vs. 13 (7.7 %) in the EUS-FNA group (P = 0.21). Three patients had recurrence in the stomach wall: one (2.6 %) patient in the non-EUS-FNA group vs. two patients (1.2 %) in EUS-FNA group (P = 0.46). A total of 16 patients had peritoneal recurrence: 5 patients (12.8 %) in the non-EUS-FNA group and 11 patients (6.5 %) in the EUS-FNA group (P = 0.19). In a multivariate analysis, undergoing EUS-FNA was not associated with increased cancer recurrence or decreased overall survival. Conclusion: Pre-operative EUS-FNA was not associated with an increased rate of gastric or peritoneal cancer recurrence in patients with resected pancreatic cancer. Two patients had gastric wall recurrence following the procedure, but this may be explained by direct tumor extension. This suggests that EUS-FNA is not associated with an increased risk of needle track seeding.

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[87]

TÍTULO / TITLE: - alpha2,3-Sialyltransferase ST3Gal IV promotes migration and metastasis in pancreatic adenocarcinoma cells and tends to be highly expressed in pancreatic adenocarcinoma tissues.

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

REVISTA / JOURNAL: - Int J Biochem Cell Biol. 2013 Aug;45(8):1748-57. doi: 10.1016/j.biocel.2013.05.015. Epub 2013 May 29.

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

1016/j.biocel.2013.05.015

AUTORES / AUTHORS: - Perez-Garay M; Arteta B; Llop E; Cobler L; Pages L; Ortiz R; Ferri MJ; de Bolos C; Figueras J; de Llorens R; Vidal-Vanaclocha F; Peracaula R

INSTITUCIÓN / INSTITUTION: - Department of Biology, University of Girona, 17071 Girona, España.

RESUMEN / SUMMARY: - Sialyltransferases have received much attention recently as they are frequently up-regulated in cancer cells. However, the role played by each sialyltransferase in tumour progression is still unknown. alpha2,3-Sialyltransferases ST3Gal III and ST3Gal IV are involved in sialyl-Lewis(x) (SLe(x)) synthesis. Given that the role of ST3Gal III in pancreatic adenocarcinoma cells has been previously reported, in this study we have focused on investigating the role of ST3Gal IV in the acquisition of adhesive, migratory and metastatic capabilities and, secondly, in analyzing the expression of ST3Gal III and ST3Gal IV in pancreatic adenocarcinoma tissues versus

control tissues. ST3Gal IV overexpressing pancreatic adenocarcinoma MDAPanc-28 cell lines were generated. They showed a heterogeneous increase in SLe(x), and enhanced E-selectin adhesion and migration. Furthermore, when injected into nude mice, increased metastasis and decreased survival were found in comparison with controls. The behaviour of MDAPanc-28 ST3Gal IV overexpressing cells in these processes was similar to the already reported MDAPanc-28 ST3Gal III overexpressing cells. Furthermore, pancreatic adenocarcinoma tissues tended to express high levels of ST3Gal III and ST3Gal IV together with other fucosyltransferase genes FUT3 and FUT6, all involved in the last steps of sialyl-Lewis(x) biosynthesis. In conclusion, both alpha2,3-sialyltransferases are involved in key steps of pancreatic tumour progression processes and are highly expressed in most pancreatic adenocarcinoma tissues.

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[88]

- CASTELLANO -

TÍTULO / TITLE: Solid pseudopapillary neoplasm of the pancreas or Frantz s tumour: Report of two cases with different locations.

TÍTULO / TITLE: - Solid pseudopapillary neoplasm of the pancreas or Frantz s tumour: Report of two cases with different locations.

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

REVISTA / JOURNAL: - Rev Esp Enferm Dig. 2013 May;105(3):176-177.

AUTORES / AUTHORS: - Verdu-Fernandez MA; Garcia-Garcia ML; Guillen-Paredes MP; Martin-Lorenzo JG; Aguayo-Albasini JL

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[89]

TÍTULO / TITLE: - Knockdown of Oct4 and Nanog expression inhibits the stemness of pancreatic cancer cells.

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

REVISTA / JOURNAL: - Cancer Lett. 2013 Jul 17. pii: S0304-3835(13)00514-4. doi: 10.1016/j.canlet.2013.07.009.

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

1016/j.canlet.2013.07.009

AUTORES / AUTHORS: - Lu Y; Zhu H; Shan H; Lu J; Chang X; Li X; Lu J; Fan X; Zhu S; Wang Y; Guo Q; Wang L; Huang Y; Zhu M; Wang Z

INSTITUCIÓN / INSTITUTION: - Surgical Comprehensive Laboratory, Affiliated Hospital of Nantong University, Nantong, Jiangsu Province 226001, PR China; Department of General Surgery, Affiliated Hospital of Nantong University, Nantong, Jiangsu Province 226001, PR China; Visitor Scholar of Wake Forest Institute for Regenerative Medicine, Wake Forest University School of Medicine, Winston-Salem, NC 27101, USA.

RESUMEN / SUMMARY: - Pancreatic cancer is notorious for its difficult diagnosis at early stage and poor recurrence-free prognosis. This study aimed to investigate the possible involvement of Oct4 and Nanog in pancreatic cancer. The high expressions of Oct4 and Nanog in human pancreatic cancer tissues were found to indicate a worse prognostic value of patients. The pancreatic cancer stem cells (PCSCs) that isolated from PANC-1 cell line by flow cytometry exhibited high expressions of Oct4 and Nanog. To investigate whether Oct4 and Nanog play crucial role in maintaining the stemness of PCSCs, double knockdown of Oct4 and Nanog demonstrated that Oct4 and Nanog significantly reduced proliferation, migration, invasion, chemoresistance, and tumorigenesis of PCSCs in vitro and in vivo. The altered expression of the genes related to pancreatic carcinogenesis, metastasis, drug resistance and epithelial-mesenchymal transdifferentiation (EMT) might affect the biological characteristics of PCSCs. Our results suggest that Oct4 and Nanog may serve as a potential marker of prognosis and a novel target of therapy for pancreatic cancer.

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[90]

TÍTULO / TITLE: - Glasgow prognostic score predicts therapeutic outcome after pancreaticoduodenectomy for carcinoma of the ampulla of vater.

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

REVISTA / JOURNAL: - Anticancer Res. 2013 Jun;33(6):2715-21.

AUTORES / AUTHORS: - Shiba H; Misawa T; Fujiwara Y; Futagawa Y; Furukawa K; Haruki K; Iwase R; Wakiyama S; Ishida Y; Yanaga K

INSTITUCIÓN / INSTITUTION: - Department of Surgery, School of Medicine, Jikei University, Minato-ku, Tokyo, Japan. hs0817@jikei.ac.jp

RESUMEN / SUMMARY: - BACKGROUND: Systemic inflammation, as evidenced by the Glasgow prognostic score (GPS), predicts cancer-specific survival in various types of cancer. The aim of this study was to evaluate the significance of GPS on the therapeutic outcome after pancreaticoduodenectomy for carcinoma of the ampulla of Vater. PATIENTS AND METHODS: The subjects of this study were 30 patients who underwent elective pancreaticoduodenectomy for carcinoma of the ampulla of Vater. For the assessment of systemic inflammatory response using the GPS, patients were classified into three groups: patients with normal albumin (>/= 3.5 g/dl) and normal C-reactive protein (CRP) (</= 1.0 mg/dl) as GPS 0 (n=23), those with low albumin (<3.5 g/dl) or elevated CRP (>1.0 mg/dl) as GPS 1 (n=5), and those with low albumin (<3.5 g/dl) and elevated CRP (>1.0 mg/dl) as GPS 2 (n=2). We retrospectively investigated the relationship between patients' characteristics, including GPS, and disease-free survival, as well as overall survival. RESULTS: For disease-free survival, advanced tumor stage (p=0.0401), advanced lymph node metastasis (p<0.0001), and preoperative biliary drainage (p=0.0157) in univariate analysis, and advanced lymph node metastasis (p=0.0271) in

multivariate analysis were significant and independent predictors of cancer recurrence. For overall survival, in both univariate and multivariate analyses, advanced lymph node metastasis (p=0.0006 and p=0.0411, respectively) and GPS 1 or 2 (p=0.0034 and p=0.0484, respectively) were significant and independent predictors of poor patient outcome. CONCLUSION: The GPS in patients with carcinoma of the ampulla of Vater is an independent prognostic predictor after elective pancreaticoduodenectomy.

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[91]

TÍTULO / TITLE: - Fibroblast growth factor receptor 1 gene amplification in pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Histopathology. 2013 Aug;63(2):157-66. doi: 10.1111/his.12115. Epub 2013 Jun 28.

●● Enlace al texto completo (gratuito o de pago) 1111/his.12115

AUTORES / AUTHORS: - Lehnen NC; von Massenhausen A; Kalthoff H; Zhou H; Glowka T; Schutte U; Holler T; Riesner K; Boehm D; Merkelbach-Bruse S; Kirfel J; Perner S; Gutgemann I

INSTITUCIÓN / INSTITUTION: - Institute of Pathology, University Hospital of Bonn, Bonn, Germany.

RESUMEN / SUMMARY: - AIMS: Pancreatic ductal adenocarcinomas (PDACs) are chemoresistant, resulting in extremely poor survival of patients; therefore, novel molecular targets, even in small subsets of genetically characterized tumours, are urgently needed. Tyrosine kinase receptor inhibitors (TKIs) are already in clinical use. The aims of this study were to examine the gene copy number and expression of fibroblast growth factor receptor 1 (FGFR1) in 155 patients with PDAC, and investigate the effects of the FGFR-specific inhibitor BGJ398 on FGFR1-amplified pancreatic tumour cells in vitro. METHODS AND RESULTS: Fluorescence in-situ hybridization (FISH) and immunohistochemical analysis of 155 PDACs were performed using tissue microarrays. Amplification of FGFR1 was found in 2.6% (4/155) of cases. Four per cent of tumours (5/125) were shown to express FGFR1 by immunohistochemistry. Sequence analysis demonstrated an activating KRAS mutation (exon 2) in all FGFR1-amplified cases. The FGFR1-amplified pancreatic carcinoma cell line PT45P1 showed high levels of FGFR1 mRNA and protein expression. Proliferation of this cell line can be inhibited using the FGFR1 inhibitor BGJ398. CONCLUSIONS: FGFR1 represents a potential new therapeutic target in a subset of patients harbouring FGFR1-amplified tumours. Identification of pancreatic cancers harbouring FGFR1 amplification may be important in preselecting patients and/or interpreting clinical studies using TKIs.

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[92]

TÍTULO / TITLE: - Role of bacterial infections in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Carcinogenesis. 2013 Jul 10.
●● Enlace al texto completo (gratuito o de pago) 1093/carcin/bgt249
AUTORES / AUTHORS: - Michaud DS
INSTITUCIÓN / INSTITUTION: - Department of Epidemiology, School of Public Health, Brown University, Providence, RI, USA.
RESUMEN / SUMMARY: - Established risk factors for pancreatic cancer, including tobacco smoking, chronic pancreatitis, obesity, and type II diabetes, collectively account for less than half of all pancreatic cancer cases. Inflammation plays a key role in pancreatic carcinogenesis, but it is unclear what causes local inflammation, other than pancreatitis. Epidemiological data suggest that Helicobacter pylori may be a risk factor for pancreatic cancer, and more recently, data suggest that periodontal disease, and Porphyromonas gingivalis, a pathogen for periodontal disease, may also play a role in pancreatic carcinogenesis. Individuals with periodontal disease have elevated markers of systemic inflammation, and oral bacteria can disseminate into the blood, stomach, heart, and even reach the brain. These infections may contribute to the progression of pancreatic cancer by acting jointly with other pancreatic cancer risk factors that impact the inflammation and immune response, such as smoking and obesity, and the ABO genetic variant, recently linked to pancreatic cancer through genome-wide association studies. The complex interplay between bacteria, host immune response, and environmental factors has been examined closely in relation to gastric cancer, but new research suggests bacteria may be playing a role in other gastrointestinal cancers. This review will summarize the literature on epidemiological studies examining infections that have been linked to pancreatic cancer and propose mechanistic pathways that may tie infections to pancreatic cancer.

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[93]
TÍTULO / TITLE: - Neoadjuvant treatment of borderline resectable and non-resectable pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Ann Oncol. 2013 Jul 12.
●● Enlace al texto completo (gratuito o de pago) 1093/annonc/mdt239
AUTORES / AUTHORS: - Heinemann V; Haas M; Boeck S
INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology and Comprehensive Cancer Center, Ludwig-Maximilians-University of Munich, Munich, Germany.
RESUMEN / SUMMARY: - Neoadjuvant therapy is increasingly becoming a valid treatment option for patients with locally advanced pancreatic cancer (LAPC). In borderline resectable disease, neoadjuvant therapy is employed to improve the probability of margin-clear resections. In non-metastatic, non-resectable

pancreatic cancer, treatment primarily aims to induce disease control, but may achieve conversion to surgical resectability in some patients. Several treatment modalities including chemotherapy, chemoradiotherapy (CRT) or the sequential use of both have been investigated in numerous, mostly small and non-randomized studies. Nevertheless, there is a consistent finding that neoadjuvant therapy can induce resectability in up to 30%-40% of LAPC patients. Once resection has been achieved, overall survival appears to be comparable to that observed for primarily resectable patients. Thus, patient selection evolves as an important aspect of neoadjuvant therapy; retrospective analyses identified induction chemotherapy as an appropriate tool to define LAPC patients who may benefit most from subsequent treatment with CRT. The clinical importance of induction chemotherapy may further increase once highly active protocols such as the FOLFIRINOX or the gemcitabine plus nab-paclitaxel regimen are introduced into novel multimodality treatment concepts.

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[94]

TÍTULO / TITLE: - Incidentally Discovered Pancreatic Intraepithelial Neoplasia: What Is Its Clinical Significance?

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Jun 8.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3042-2

AUTORES / AUTHORS: - Konstantinidis IT; Vinuela EF; Tang LH; Klimstra DS; D'Angelica MI; Dematteo RP; Kingham TP; Fong Y; Jarnagin WR; Allen PJ

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

RESUMEN / SUMMARY: - PURPOSE: Pancreatic intraepithelial neoplasia (PanIN) is a presumed precursor of pancreatic ductal adenocarcinoma (PDAC). We assessed the relationship between incidental PanIN after resection of non-adenocarcinoma lesions and the development of metachronous PDAC in the remnant. METHODS: We retrospectively reviewed the clinicopathologic data of patients who underwent pancreatectomy for non-PDAC from January 2000 to January 2010. Intraductal papillary mucinous lesions were excluded. All available postoperative imaging and clinical follow-up data were reviewed; the risk of developing PDAC was assessed in patients with a minimum follow-up time of 6 months and with imaging studies available for review. RESULTS: A total of 584 patients were analyzed. Median age was 59 years (range 10-85 years), and 338 (58 %) were female. The most common lesions for which resection was performed were serous cystic neoplasms (17 %), pancreatic neuroendocrine tumors (38 %), metastatic tumors (9 %), and mucinous cystic neoplasms (7 %). PanIN was identified in 153 (26 %) patients. The majority of these patients had PanIN-1 or -2 (50 and 41 %, respectively), whereas 13 (8 %) had PanIN-3. Of the 506 (87 %) patients with adequate follow-up (median 3.7

years, range 0.5-12.6 years), 1 patient (0.2 %) with PanIN identified at the time of initial resection developed cancer in the remnant. This occurred 4.4 years after a distal pancreatectomy in the setting of PanIN-1B. No patient with PanIN-3 developed cancer during follow-up. CONCLUSIONS: PanIN was identified in 26 % of patients who underwent resection for histopathology other than PDAC. The presence of PanIN of any grade did not result in an appreciable cancer risk in the pancreatic remnant after short-term follow-up.

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[95]

TÍTULO / TITLE: - Impact of Octreotide LAR on Tumour Growth Control as First-Line Treatment in Neuroendocrine Tumours of Pancreatic Origin.

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

REVISTA / JOURNAL: - Neuroendocrinology. 2013 Jun 22.

●● Enlace al texto completo (gratuito o de pago) 1159/000353785

AUTORES / AUTHORS: - Jann H; Denecke T; Koch M; Pape UF; Wiedenmann B; Pavel M

INSTITUCIÓN / INSTITUTION: - Departments of Hepatology and Gastroenterology, Charite, Berlin, Germany.

RESUMEN / SUMMARY: - Background: Somatostatin analogues (SSA) are widely used in treatment of patients with functioning and non-functioning neuroendocrine tumours (NET). The aim of our investigation was to evaluate the antiproliferative effect of SSA in patients with pancreatic NET. Methods: We retrospectively analyzed records of 43 patients with pancreatic NET treated at our clinic with octreotide LAR as first-line therapy. The aim of our study was to investigate the overall best response according to RECIST criteria, overall best response defined as disease control rate (SD+PR), response and disease control rate at 12 months as well as time to progression (TTP). Results: Mean age (+/- SD) of the patients (16 female symbol/27 male symbol) at initial diagnosis was 54.7 +/- 11.86 years. At start of therapy 39 of 43 patients were classified as stage IV according to ENETS-TNM. Tumours were graded, based on MiB-1/Ki67 staining, as G1 (n = 8) and G2 (n = 30); unknown (n = 5). Octreoscan was positive in 37 patients, negative in 2 and unknown in 4 cases. 19 patients had functioning tumours, 24 patients had non-functioning tumours. Median overall survival was 98 months, median TTP was 13 months. Analysis of grading showed a statistically significant influence on TTP when comparing the median TTP for Ki67 >10% with Ki67< 5% (p = 0.009) and Ki67 5-10% (p = 0.036). Conclusion: SSA may be considered as first-line treatment for antiproliferative purposes in metastatic NET of the pancreas. Patients with a proliferation index of less than 10% displayed a more durable response compared to those with a higher proliferation index. © 2013 S. Karger AG, Basel.

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[96]
TÍTULO / TITLE: - Proteins differentially expressed in human beta-cells-enriched pancreatic islet cultures and human insulinomas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Mol Cell Endocrinol. 2013 Jul 24. pii: S0303-7207(13)00287-6. doi: 10.1016/j.mce.2013.07.004.
●● Enlace al texto completo (gratuito o de pago) 1016/j.mce.2013.07.004
AUTORES / AUTHORS: - Terra LF; Teixeira PC; Wailemann RA; Zelanis A; Palmisano G; Cunha-Neto E; Kalil J; Larsen MR; Labriola L; Sogayar MC
INSTITUCIÓN / INSTITUTION: - Instituto de Quimica, Departamento de Bioquimica, Universidade de Sao Paulo (USP), Sao Paulo, Brazil.
RESUMEN / SUMMARY: - In view of the great demand for human beta-cells for physiological and medical studies, we generated cell lines derived from human insulinomas which secrete insulin, C-peptide and express neuroendocrine and islet markers. In this study, we set out to characterize their proteomes, comparing them to those of primary beta-cells using DIGE followed by MS. The results were validated by Western blotting. An average of 1800 spots was detected with less than 1% exhibiting differential abundance. Proteins more abundant in human islets, such as Caldesmon, are involved in the regulation of cell contractility, adhesion dependent signaling, and cytoskeletal organization. In contrast, almost all proteins more abundant in insulinoma cells, such as MAGE2, were first described here and could be related to cell survival and resistance to chemotherapy. Our proteomic data provides, for the first time, a molecular snapshot of the orchestrated changes in expression of proteins involved in key processes which could be correlated with the altered phenotype of human beta-cells. Collectively our observations prompt research towards the establishment of bioengineered human beta-cells providing a new and needed source of cultured human beta-cells for beta-cell research, along with the development of new therapeutic strategies for detection, characterization and treatment of insulinomas.

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[97]
TÍTULO / TITLE: - S100A2 is a predictive biomarker of adjuvant therapy benefit in pancreatic adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Eur J Cancer. 2013 Aug;49(12):2643-2653. doi: 10.1016/j.ejca.2013.04.017. Epub 2013 May 28.
●● Enlace al texto completo (gratuito o de pago) 1016/j.ejca.2013.04.017
AUTORES / AUTHORS: - Bachet JB; Marechal R; Demetter P; Bonnetain F; Cros J; Svrcek M; Bardier-Dupas A; Hammel P; Sauvanet A; Louvet C; Paye F; Vaillant JC; Andre T; Closset J; Salmon I; Emile JF; Van Laethem JL
INSTITUCIÓN / INSTITUTION: - Medical University Pierre et Marie Curie, UFR Paris VI, 91-105 Boulevard de l'Hopital, 75634 Paris, France; EA4340

“Epidemiologie et oncogenese des tumeurs digestives”, Faculte de medecine PIFO, UVSQ, 9 Boulevard d’Alembert, 78280 Guyancourt, France; Department of Hepatogastroenterology, Pitie Salpetriere Hospital, APHP, 47-83 Boulevard de l’hopital, 75651 Paris Cedex 13, France; Department of Gastroenterology and Gastrointestinal Cancer Unit, Erasme Hospital, ULB, 808 Route de Lennik, 1070 Bruxelles, Belgium. Electronic address: jean-baptiste.bachet@psl.aphp.fr.

RESUMEN / SUMMARY: - BACKGROUND: Prognosis of patients with pancreatic adenocarcinoma (PAC) remains poor. S100A2 has been recently suggested as a negative prognostic biomarker in PAC. We aimed to investigate its prognostic and/or predictive value in a large independent multicentric cohort of patients with resected PAC. METHODS: Sequential samples of 471 patients were retrospectively collected; 142 patients did not receive adjuvant treatment (30%) and 329 (70%) received an adjuvant treatment. We measured protein levels of S100A2 by semiquantitative immunohistochemistry with tissue microarrays and correlated with patients’ overall survival (OS) and disease-free survival (DFS). RESULTS: S100A2 protein status was obtained in 462 (98%) patients. Its expression was low, moderate or high in 59%, 12% and 2% of cases, respectively. It was not correlated with DFS or OS in the whole population, neither in the subgroup of patients who did not receive adjuvant treatment. However among patients who received an adjuvant therapy, moderate/high levels of S100A2 were significantly associated with longer OS and DFS in multivariate analysis (hazard ratios of 0.63, p=0.022 and 0.67, p=0.017, respectively), whereas low S100A2 was not. Interaction tests for adjuvant therapy were statistically significant both for the OS and the DFS (p=0.001 and p=0.023, respectively). On multivariate analysis, S100A2 retained independent predictive values (OS: p<0.001, DFS: p=0.003) with a significant benefit of adjuvant therapy for those patients with moderate/high S100A2. CONCLUSIONS: S100A2 expression predicts longer DFS and OS in patients treated with adjuvant therapy and should be evaluated as a predictive biomarker.

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[98]

TÍTULO / TITLE: - The immune network in pancreatic cancer development and progression.

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

REVISTA / JOURNAL: - Oncogene. 2013 Jul 15. doi: 10.1038/onc.2013.257.

●● Enlace al texto completo (gratuito o de pago) 1038/onc.2013.257

AUTORES / AUTHORS: - Wormann SM; Diakopoulos KN; Lesina M; Algul H

INSTITUCIÓN / INSTITUTION: - Medizinische Klinik, Klinikum rechts der Isar, Technische Universitat Munchen, Munich, Germany.

RESUMEN / SUMMARY: - The presence of stromal desmoplasia is a hallmark of spontaneous pancreatic ductal adenocarcinoma, forming a unique microenvironment that comprises many cell types. Only recently, the immune

system has entered the pathophysiology of pancreatic ductal adenocarcinoma development. Tumor cells in the pancreas seem to dysbalance the immune system, thus facilitating spontaneous cancer development. This review will try to assemble all relevant data to demonstrate the implications of the immune network on spontaneous cancer development.Oncogene advance online publication, 15 July 2013; doi:10.1038/onc.2013.257.

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[99]

TÍTULO / TITLE: - EVI1 oncogene promotes KRAS pathway through suppression of microRNA-96 in pancreatic carcinogenesis.

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

REVISTA / JOURNAL: - Oncogene. 2013 Jun 10. doi: 10.1038/onc.2013.204.

●● Enlace al texto completo (gratuito o de pago) 1038/onc.2013.204

AUTORES / AUTHORS: - Tanaka M; Suzuki HI; Shibahara J; Kunita A; Isagawa T; Yoshimi A; Kurokawa M; Miyazono K; Aburatani H; Ishikawa S; Fukayama M

INSTITUCIÓN / INSTITUTION: - Department of Pathology, University of Tokyo, Tokyo, Japan.

RESUMEN / SUMMARY: - Despite frequent KRAS mutation, the early molecular mechanisms of pancreatic ductal adenocarcinoma (PDAC) development have not been fully elucidated. By tracking a potential regulator of another feature of PDAC precursors, acquisition of foregut or gastric epithelial gene signature, we herein report that aberrant overexpression of ecotropic viral integration site 1 (EVI1) oncoprotein, which is usually absent in normal pancreatic duct, is a widespread marker across the full spectrum of human PDAC precursors and PDAC. In pancreatic cancer cells, EVI1 depletion caused remarkable inhibition of cell growth and migration, indicating its oncogenic roles. Importantly, we found that EVI1 upregulated KRAS expression through suppression of a potent KRAS suppressor, miR-96, in pancreatic cancer cells. Collectively, the present findings suggest that EVI1 overexpression and KRAS mutation converge on activation of the KRAS pathway in early phases of pancreatic carcinogenesis and propose EVI1 and/or miR-96 as early markers and therapeutic targets in this dismal disease.Oncogene advance online publication, 10 June 2013; doi:10.1038/onc.2013.204.

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[100]

TÍTULO / TITLE: - Development of a New Thiol Site-Specific Prosthetic Group and Its Conjugation with [Cys]-exendin-4 for in Vivo Targeting of Insulinomas.

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

REVISTA / JOURNAL: - Bioconjug Chem. 2013 Jun 28.

●● Enlace al texto completo (gratuito o de pago) 1021/bc400084u

AUTORES / AUTHORS: - Yue X; Kiesewetter DO; Guo J; Sun Z; Zhang X; Zhu L; Niu G; Ma Y; Lang L; Chen X

INSTITUCIÓN / INSTITUTION: - National Institute of Biomedical Imaging and Bioengineering (NIBIB), National Institutes of Health (NIH) , 31 Center Drive, Bethesda, Maryland 20892, United States.

RESUMEN / SUMMARY: - A new tracer, N-5-[18F]fluoropentylmaleimide ([18F]FPenM), for site-specific labeling of free thiol group in proteins and peptides was developed. The tracer was synthesized in three steps (18F displacement of the aliphatic tosylate, di-Boc removal by TFA to expose free amine, and incorporation of the free amine into a maleimide). The radiosynthesis was completed in 110 min with 11-17% radiochemical yield (uncorrected), and specific activity of 20-49 GBq/mumol. [18F]FPenM showed comparable labeling efficiency with N-[2-(4-[18F]fluorobenzamido)ethyl]maleimide ([18F]FBEM). Its application was demonstrated by conjugation with glucagon-like peptide type 1 (GLP-1) analogue [cys40]-exendin-4. The cell uptake, binding affinity, imaging properties, biodistribution, and metabolic stability of the radiolabeled [18F]FPenM-[cys40]-exendin-4 were studied using INS-1 tumor cells and INS-1 xenograft model. Positron emission tomography (PET) results showed that the new thiol-specific tracer, [18F]FPenM-[cys40]-exendin-4, had high tumor uptake (20.32 +/- 4.36%ID/g at 60 min postinjection) and rapid liver and kidney clearance, which was comparable to the imaging results with [18F]FBEM-[cys40]-exendin-4 reported by our group.

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[101]

TÍTULO / TITLE: - Insulinoma-associated 1ª (Insm1a) is required for photoreceptor differentiation in the zebrafish retina.

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

REVISTA / JOURNAL: - Dev Biol. 2013 Aug 15;380(2):157-71. doi: 10.1016/j.ydbio.2013.05.021. Epub 2013 Jun 4.

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

1016/j.ydbio.2013.05.021

AUTORES / AUTHORS: - Forbes-Osborne MA; Wilson SG; Morris AC

INSTITUCIÓN / INSTITUTION: - Department of Biology, University of Kentucky, Lexington, KY 40506-0225, USA.

RESUMEN / SUMMARY: - The zinc-finger transcription factor insulinoma-associated 1 (Insm1, previously IA-1) is expressed in the developing nervous and neuroendocrine systems, and is required for cell type specific differentiation. Expression of Insm1 is largely absent in the adult, although it is present in neurogenic regions of the adult brain and zebrafish retina. While expression of Insm1 has also been observed in the embryonic retina of numerous vertebrate species, its function during retinal development has remained unexplored. Here, we demonstrate that in the developing zebrafish retina, insm1a is required for photoreceptor differentiation. Insm1a-deficient embryos were microphthalmic and displayed defects in rod and cone

photoreceptor differentiation. Rod photoreceptor cells were more sensitive to loss of insm1a expression than were cone photoreceptor cells. Additionally, we provide evidence that insm1a regulates cell cycle progression of retinoblasts, and functions upstream of the bHLH transcription factors ath5/atoh7 and neurod, and the photoreceptor specification genes crx and nr2e3. Finally, we show that insm1a is negatively regulated by Notch-Delta signaling. Taken together, our data demonstrate that Insm1 influences neuronal subtype differentiation during retinal development.

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[102]

TÍTULO / TITLE: - Performance characteristics of molecular (DNA) analysis for the diagnosis of mucinous pancreatic cysts.

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

REVISTA / JOURNAL: - Gastrointest Endosc. 2013 Jul 9. pii: S0016-5107(13)01985-8. doi: 10.1016/j.gie.2013.05.026.

●● Enlace al texto completo (gratuito o de pago) 1016/j.gie.2013.05.026

AUTORES / AUTHORS: - Al-Haddad M; Dewitt J; Sherman S; Schmidt CM; Leblanc JK; McHenry L; Cote G; El Chafic AH; Luz L; Stuart JS; Johnson CS; Klochan C; Imperiale TF

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

RESUMEN / SUMMARY: - BACKGROUND: Diagnosis of mucinous pancreatic cysts (MPCs) is challenging due to the poor sensitivity of cytology provided by EUS-guided-FNA (EUS-FNA). OBJECTIVE: To quantify the test characteristics of molecular (DNA) analysis in suspected low-risk MPCs. DESIGN: A prospective cohort study performed in between 2008 and 2011. SETTING: Academic referral center. PATIENTS: Consecutive patients who underwent EUS-FNA of suspected MPCs. INTERVENTION: EUS-FNA and molecular (DNA) analysis of cyst fluid. MAIN OUTCOME MEASUREMENTS: The sensitivity and specificity of molecular analysis in the diagnosis of MPCs using the criterion standard of surgical pathology in resected cysts. RESULTS: Patients with suspected MPCs underwent EUS-FNA and cyst fluid DNA analysis. Surgical resection was performed in 48 patients (17%), confirming a mucinous pathology in 38 (79%). In this group, molecular analysis had a sensitivity of 50% and a specificity of 80% in identifying MPCs (accuracy of 56.3%). The combination of molecular analysis with cyst fluid carcinoembryonic antigen (CEA) and cytology resulted in higher MPC diagnostic performance than either one of its individual components, with a sensitivity, specificity, and accuracy of 73.7%, 70%, and 72.9%, respectively. There was no significant difference in accuracy between molecular analysis and CEA/cytology in this group. LIMITATIONS: Single-center experience. CONCLUSION: Molecular analysis aids in the diagnosis of MPCs when cytology is nondiagnostic or cyst fluid is insufficient for CEA or its level is indeterminate. Our results do not

support the routine use of molecular analysis, which should be used selectively after review of imaging findings and cyst fluid studies. Further studies are needed to assess DNA's performance in malignant cysts.

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[103]
TÍTULO / TITLE: - Serum miR-1290 as a marker of pancreatic cancer - Letter.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Cancer Res. 2013 Jul 25.
●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-1620
AUTORES / AUTHORS: - Frampton AE; Krell J; Kazemier G; Giovannetti E
INSTITUCIÓN / INSTITUTION: - Department of Surgery & Cancer, Imperial College.
RESUMEN / SUMMARY: - na.

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[104]
TÍTULO / TITLE: - Serum miR-1290 as a marker of pancreatic cancer - Response.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Cancer Res. 2013 Jul 23.
●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-13-1899
AUTORES / AUTHORS: - Li A; Yu J; Kim H; Wolfgang C; Canto M; Hruban RH; Goggins M
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Medicine and Oncology, The Johns Hopkins Medical Institutions.
RESUMEN / SUMMARY: - Not applicable.

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[105]
TÍTULO / TITLE: - SB365, Pulsatilla saponin D suppresses proliferation and induces apoptosis of pancreatic cancer cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Oncol Rep. 2013 Aug;30(2):801-8. doi: 10.3892/or.2013.2517. Epub 2013 Jun 4.
●● Enlace al texto completo (gratuito o de pago) 3892/or.2013.2517
AUTORES / AUTHORS: - Son MK; Jung KH; Lee HS; Lee H; Kim SJ; Yan HH; Ryu YL; Hong SS
INSTITUCIÓN / INSTITUTION: - Department of Drug Development, College of Medicine, Inha University, Sinheungdong, Jung-gu, Incheon 400-712, Republic of Korea.
RESUMEN / SUMMARY: - Pulsatilla koreana has been used as a traditional medicine for the treatment of various diseases. The purpose of this study was to

determine whether SB365, Pulsatilla saponin D isolated from the root of Pulsatilla koreana inhibits the progression of pancreatic cancer. We found that SB365 strongly suppressed the growth and proliferation of 5 human pancreatic cancer cell lines (MIAPaCa-2, BXPC-3, PANC-1, AsPC-1 and HPAC). The apoptotic effect of SB365 was demonstrated by increased levels of cleaved caspase-3 and decreased Bcl-2 expression via mitochondrial membrane potential, as well as elevated numbers of terminal deoxynucleotidyl-transferase-mediated dUTP nick end labeling (TUNEL)-positive apoptotic cells. SB365 was also found to exert an anti-angiogenic effect by decreasing the expression of HIF-1alpha and VEGF, major factors of angiogenesis, which was confirmed by the suppression of tumor sphere formation of pancreatic cancer cells. An in vivo mouse xenograft study showed that SB365 significantly inhibited tumor growth through the induction of apoptosis and inhibition of angiogenesis with strong anticancer activity. Therefore, SB365 is a good candidate as a natural product for use in the treatment of pancreatic cancer.

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[106]

TÍTULO / TITLE: - Impact of Adjuvant Radiotherapy on Survival after Pancreatic Cancer Resection: An Appraisal of Data from the National Cancer Data Base.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Jun 15.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3047-x

AUTORES / AUTHORS: - Kooby DA; Gillespie TW; Liu Y; Byrd-Sellers J; Landry J; Bian J; Lipscomb J

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Emory University School of Medicine, Atlanta, GA, USA, dkooby@emory.edu.

RESUMEN / SUMMARY: - PURPOSE: The impact of adjuvant radiotherapy for pancreatic adenocarcinoma (PAC) remains controversial. We examined effects of adjuvant therapy on overall survival (OS) in PAC, using the National Cancer Data Base (NCDB). METHODS: Patients with resected PAC from 1998 to 2002 were queried from the NCDB. Factors associated with receipt of adjuvant chemotherapy (ChemoOnly) versus adjuvant chemoradiotherapy (ChemoRad) versus no adjuvant treatment (NoAdjuvant) were assessed. Cox proportional hazard modeling was used to examine effect of adjuvant therapy type on OS. Propensity scores (PS) were developed for each treatment arm and used to produce matched samples for analysis to minimize selection bias. RESULTS: From 1998 to 2002, a total of 11,526 patients underwent resection of PAC. Of these, 1,029 (8.9 %) received ChemoOnly, 5,292 (45.9 %) received ChemoRad, and 5,205 (45.2 %) received NoAdjuvant. On univariate analysis, factors associated with improved OS included: younger age, higher income, higher facility volume, lower tumor stage and grade, negative margins and nodes, and absence of adjuvant therapy. On multivariate analysis with matched PS, factors

independently associated with improved OS included: younger age, higher income, higher facility volume, later year of diagnosis, smaller tumor size, lower tumor stage, and negative tumor margins and nodes. ChemoRad had the best OS (hazard ratio 0.70, 95 % confidence interval 0.61-0.80) in a PS matched comparison with ChemoOnly (hazard ratio 1.04, 95 % confidence interval 0.93-1.18) and NoAdjuvant (index). CONCLUSIONS: Adjuvant chemotherapy with radiotherapy is associated with improved OS after PAC resection in a large population from the NCDB. On the basis of these analyses, radiotherapy should be a part of adjuvant therapy for PAC.

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[107]

TÍTULO / TITLE: - Non-invasive quantification of anti-angiogenic therapy by contrast-enhanced MRI in experimental pancreatic cancer.

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

REVISTA / JOURNAL: - Acta Radiol. 2013 Jul 26.

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

1177/0284185113493776

AUTORES / AUTHORS: - Raatschen HJ; Fischer S; Zsivcsec B; Schoenfeld CO; Hotz B; Buhr HJ; Hotz HG

INSTITUCIÓN / INSTITUTION: - Department of Diagnostic and Interventional Radiology, Hannover Medical School, Hannover, Germany.

RESUMEN / SUMMARY: - BACKGROUND: Currently, early changes of tumor vasculature after angiogenesis inhibition can only be evaluated by histopathology, a method not suitable in a clinical setting. PURPOSE: To quantify effects of different angiogenesis inhibitors on the microvasculature of orthotopically implanted pancreatic cancers by contrast-enhanced magnetic resonance imaging (MRI) in order to establish a non-invasive technique for monitoring antiangiogenic cancer treatment. MATERIAL AND METHODS: DSL-6ª/C1 pancreatic cancers were implanted in the pancreas of 109 Lewis rats. Three weeks later, antiangiogenic treatment was initiated by administration of Bevacizumab (n = 38) or Suramin (n = 27) while the control group (n = 44) remained untreated. Dynamic MRI was performed 24 h, 1 week, and 4 weeks after treatment initiation. Fractional tumor plasma volume (fPV, %) and vascular permeability (KPS, mL/min/100 cc) were calculated based on the MRI data by using a pharmacokinetic model. RESULTS: Twenty-four hours after the initial dose, a significant decline in KPS was observed in the Bevacizumab group compared to the control and Suramin group (0.002 +/- 0.008; 0.057 +/- 0.046 and 0.064 +/- 0.062 (mean +/- SD); $P < 0.05$). At 1 week, fPV was significantly smaller in Bevacizumab and Suramin treated tumors compared to control tumors (6.25 +/- 2.74, 7.47 +/- 3.44, and 15.10 +/- 9.97, respectively; $P < 0.05$). Differences in tumor volumes were first observed after 4 weeks of treatment with significantly larger control tumors (4380.3 +/- 1590.6 vs. 869.6 +/- 717.2 and 1676.5 +/- 2524.1 mm3; $P < 0.05$). CONCLUSION: Dynamic MRI can

quantify antiangiogenic effects on tumor microvasculature before changes in tumor volumes are detectable. Thus, this technique is a reasonable addition to morphological MRI and may be applied as an alternative to histopathology.

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[108]

TÍTULO / TITLE: - Localization of the anti-cancer peptide EGFR-lytic hybrid peptide in human pancreatic cancer BxPC-3 cells by immunocytochemistry.

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

REVISTA / JOURNAL: - J Pept Sci. 2013 Aug;19(8):511-5. doi: 10.1002/psc.2529. Epub 2013 Jul 1.

●● Enlace al texto completo (gratuito o de pago) 1002/psc.2529

AUTORES / AUTHORS: - Ohara K; Kohno M; Kawakami K

INSTITUCIÓN / INSTITUTION: - Department of Pharmacoepidemiology, Graduate School of Medicine and Public Health, Kyoto University, Japan Yoshidakonoecho, Sakyoku, Kyoto city, Kyoto, 606-8501, Japan.

RESUMEN / SUMMARY: - Cationic lytic-type peptides have been studied for clinical application in various infections and cancers, but their functional cellular mechanisms remain unclear. We generated anti-cancer epithelial growth factor receptor (EGFR)-lytic hybrid peptide, a 32-amino-acid peptide composed of an EGFR-binding sequence and lytic sequence. In this study, we investigated the distribution of EGFR-lytic hybrid peptide in BxPC-3 human pancreatic cancer cells by an immunocytochemical (ICC) method. Distribution of EGFR protein expression was unchanged after treatment with EGFR-lytic peptide compared with non-treated cells. In confocal laser scanning microscopy, immunostaining of EGFR-lytic peptide was observed in the cytoplasm, mostly in the form of granules. Some staining was also localized on the mitochondrial membrane. At the ultrastructure level, cells treated with EGFR-lytic peptide had a low electron density, disappearance of microvilli, and swollen mitochondria. Fragments of cell membrane were also observed in the proximity of the membrane. In immunoelectron microscopy, EGFR-lytic peptide was observed in the cell membrane and cytoplasm. A number of granules were considered swollen mitochondria. Activation of the caspase pathway as a result of mitochondrial dysfunction was also examined to determine the cytotoxic activity of EGFR-lytic peptide; however, no effect on cell death after EGFR-lytic treatment was observed, and moreover, apoptosis was not found to play a critical role in the cell death mechanism. These results suggest that EGFR-lytic peptide is localized on cell and mitochondrial membranes, with disintegration of the cell membrane contributing mainly to cell death.

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[109]

TÍTULO / TITLE: - Association between X-ray repair cross-complementation group 1 rs25487 polymorphism and pancreatic cancer risk.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Jun 27.

●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-0914-9

AUTORES / AUTHORS: - Jiang H; Wu D; Ma D; Lin G; Liang J; Jin J

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, The Fourth Affiliated Hospital of China Medical University, No.4 Chongshandong Street, Huanggu District, Shenyang, 110032, China.

RESUMEN / SUMMARY: - Previous published studies suggested that genetic polymorphisms in DNA repair genes could modify the DNA repair capacity and could be associated with pancreatic cancer risk. However, previous studies on the association between X-ray repair cross-complementation group 1 (XRCC1) rs25487 (Arg399Gln) polymorphism and pancreatic cancer risk reported inconsistent results. To obtain a more precise estimation of the association between XRCC1 rs25487 polymorphism and pancreatic cancer risk, we performed a meta-analysis of previous published studies by calculating the pooled odds ratio (OR) with a 95 % confidence interval (95 % CI). Eight individual studies with 5,542 subjects from six publications were finally included into this meta-analysis. The meta-analysis of total eight studies showed that there was no association between XRCC1 rs25487 polymorphism and pancreatic cancer risk in total population under all four genetic models (Gln versus Arg: OR = 1.10, 95 % CI 0.95-1.28, P = 0.199; GlnGln versus ArgArg: OR = 1.15, 95 % CI 0.93-1.41, P = 0.191; GlnGln/ArgGln versus ArgArg: OR = 1.10, 95 % CI 0.97-1.25, P = 0.127; GlnGln versus ArgArg/ArgGln: OR = 1.12, 95 % CI 0.92-1.36, P = 0.253). Subgroup analysis showed that there was no association between XRCC1 rs25487 polymorphism and pancreatic cancer risk in Caucasians, but XRCC1 rs25487 polymorphism was associated with pancreatic cancer risk in Asians (GlnGln/ArgGln versus ArgArg: OR = 1.24, 95 % CI 1.01-1.53, P = 0.040). Therefore, the meta-analysis suggests that XRCC1 rs25487 polymorphism is associated with pancreatic cancer risk in Asians. Further studies with more participants are needed to provide a more precise estimation on the association above.

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[110]

TÍTULO / TITLE: - Metformin inhibits pancreatic cancer cell and tumor growth and downregulates Sp transcription factors.

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

REVISTA / JOURNAL: - Carcinogenesis. 2013 Aug 1.

●● Enlace al texto completo (gratuito o de pago) 1093/carcin/bgt231

AUTORES / AUTHORS: - Nair V; Pathi S; Jutooru I; Sreevalsan S; Basha R; Abdelrahim M; Samudio I; Safe S

INSTITUCIÓN / INSTITUTION: - Department of Veterinary Physiology and Pharmacology, Texas A&M University, College Station, TX 77843, USA.
RESUMEN / SUMMARY: - Metformin is a widely used antidiabetic drug, and epidemiology studies for pancreatic and other cancers indicate that metformin exhibits both chemopreventive and chemotherapeutic activities. Several metformin-induced responses and genes are similar to those observed after knockdown of specificity protein (Sp) transcription factors Sp1, Sp3 and Sp4 by RNA interference, and we hypothesized that the mechanism of action of metformin in pancreatic cancer cells was due, in part, to downregulation of Sp transcription factors. Treatment of Panc1, L3.6pL and Panc28 pancreatic cancer cells with metformin downregulated Sp1, Sp3 and Sp4 proteins and several pro-oncogenic Sp-regulated genes including bcl-2, survivin, cyclin D1, vascular endothelial growth factor and its receptor, and fatty acid synthase. Metformin induced proteasome-dependent degradation of Sps in L3.6pL and Panc28 cells, whereas in Panc1 cells metformin decreased microRNA-27^{a} and induced the Sp repressor, ZBTB10, and disruption of miR-27^{a}:ZBTB10 by metformin was phosphatase dependent. Metformin also inhibited pancreatic tumor growth and downregulated Sp1, Sp3 and Sp4 in tumors in an orthotopic model where L3.6pL cells were injected directly into the pancreas. The results demonstrate for the first time that the anticancer activities of metformin are also due, in part, to downregulation of Sp transcription factors and Sp-regulated genes.

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[111]
TÍTULO / TITLE: - Inhibiting K-ras Signaling Reserves the Epithelial-Mesenchymal Transition of Pancreatic Cancer Cells and its Mechanisms.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Jun;60(125):1169-73. doi: 10.5754/hge12902.
●● Enlace al texto completo (gratuito o de pago) 5754/hge12902
AUTORES / AUTHORS: - Liu XE; Sun XD
RESUMEN / SUMMARY: - Background/Aims: To investigate the effects of K-ras siRNA on pancreatic cancer cells and the expression levels of GLI1, E-cadherin and vimentin in pancreatic cancer cells transfected with K-ras siRNA. Methodology: Ppancreatic cancer cells PANC-1 were transfected with K-ras siRNA. Growth inhibition ratio of the cells were measured by MTT assay, apoptosis was detected by flow cytometery, expression level of GLI1, E-cadherin and vimentin were detected by Western blot. Results: The expression of K-ras protein was efficiently inhibited by K-ras siRNA in PANC-1 cells. The growth inhibition rates of the cells were significantly different to the control groups. Apoptosis rates were significantly different with that of control group. The expression of GLI1 was significantly down-regulated, E-cadherin was up-regulated, while vimentin was also down-regulated in K-ras siRNA transfected

cells compared with that of control groups. Conclusions: Inhibiting K-ras signaling by K-ras siRNA can inhibit proliferation and induce apoptosis of pancreatic cancer cells, down-regulate GLI1's and vimentin's expression, and up-regulate E-cadherin's expression. Inhibiting K-ras signaling by K-ras siRNA may reduce epithelial to mesenchymal transition of pancreatic cancer cell PANC-1.

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[112]

TÍTULO / TITLE: - Antiproliferative Effect of 1alpha,25-dihydroxyvitamin D3 Involves Upregulation of Cyclin-Dependent Kinase Inhibitor p21 in Human Pancreatic Cancer Cells.

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

REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Jun;60(125):1199-205. doi: 10.5754/hge11073.

●● Enlace al texto completo (gratuito o de pago) 5754/hge11073

AUTORES / AUTHORS: - Kanemaru M; Maehara N; Chijiiwa K

RESUMEN / SUMMARY: - Background/Aims: The aim of this study was to investigate the effect of 1alpha,25-dihydroxyvitamin D3 on proliferation of human pancreatic cancer cell lines and to identify related cell cycle regulatory proteins with antiproliferative effects. Methodology: Human pancreatic cancer cell lines SUIT-2 and its four sublines, and Panc-1, AsPC-1, and MiaPaCa-2 were treated with1alpha,25-dihydroxyvitamin D3. The number of cells was measured by the MTT method, and the cell cycle regulatory proteins were then analyzed by Western blotting. Results: Eight human pancreatic cancer cell lines expressed vitamin D receptor (VDR) mRNA. 1alpha,25-dihydroxyvitamin D3 inhibited proliferation of SUIT-2 and its sublines. We found p21 to be upregulated after 24 hours in S2-028, the cell line in which proliferation was most inhibited by 1alpha,25-dihydroxyvitamin D3. Conclusions: 1alpha,25-dihydroxyvitamin D3 inhibited proliferation of pancreatic cancer cells and is involved in the upregulation of cyclin-dependent kinase inhibitor p21.

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[113]

TÍTULO / TITLE: - Hypoxia induces the overexpression of microRNA-21 in pancreatic cancer cells.

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

REVISTA / JOURNAL: - J Surg Res. 2013 May 18. pii: S0022-4804(13)00433-2. doi: 10.1016/j.jss.2013.04.061.

●● Enlace al texto completo (gratuito o de pago) 1016/j.jss.2013.04.061

AUTORES / AUTHORS: - Mace TA; Collins AL; Wojcik SE; Croce CM; Lesinski GB; Bloomston M

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, The Ohio State University, Columbus, Ohio.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer cells exist in a hypoxic microenvironment containing numerous factors that impact tumor survival, proliferation, and metastasis. MicroRNAs (miRs) are differentially expressed in cancer but also altered by hypoxia. We hypothesized that hypoxia could induce expression of miR-21, an oncomir in pancreatic cancer cells. MATERIALS AND METHODS: We examined how hypoxia regulates miR-21 expression in pancreatic cancer cell lines (BxPC-3, AsPC-1) by stem-loop RT-PCR. Chromatin immunoprecipitation assays were used to study how hypoxia alters hypoxia-inducible factor (HIF)-1alpha binding to the hypoxia response element of miR-21. BxPC-3 and AsPC-1 cells were transfected with a constitutively stable HIF-1alpha subunit or vector control (pcDNA3.1) to determine the influence of miR-21 in normoxia. The effect of mature miR-21 sense and antisense oligonucleotides on proliferation and apoptosis in hypoxic and normoxic conditions was assessed via WST-1 assay and flow cytometry. RESULTS: MiR-21 levels increased in all cell lines grown in hypoxic conditions versus normoxia, whereas siRNA targeting HIF-1alpha reduced miR-21 expression. Hypoxic conditions resulted in direct binding of HIF-1alpha to the predicted binding site in miR-21. Transfection with a constitutively stable HIF-1alpha expression plasmid in normoxia resulted in upregulated miR-21, similar to that seen in hypoxia. Cells transfected with antisense constructs targeting miR-21 had reduced proliferation and increased apoptosis in normoxia, whereas miR-21 overexpression abrogated hypoxia-associated reductions in proliferation. CONCLUSIONS: MiR-21 is induced by hypoxia in pancreatic cancer cells via HIF-1alpha upregulation. MiR-21 overexpression allows cells to avoid apoptosis in a hypoxic microenvironment. Inhibition of miR-21 expression may increase cellular susceptibility to hypoxia in pancreatic cancer.

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[114]

TÍTULO / TITLE: - The Differential Effects of Statins on the Risk of Developing Pancreatic Cancer: A Case-Control Study in Two Centres in the United Kingdom.

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

REVISTA / JOURNAL: - Dig Dis Sci. 2013 Jul 18.

●● Enlace al texto completo (gratuito o de pago) 1007/s10620-013-2778-7

AUTORES / AUTHORS: - Carey FJ; Little MW; Pugh TF; Ndokera R; Ing H; Clark A; Dennison A; Metcalfe MS; Robinson RJ; Hart AR

INSTITUCIÓN / INSTITUTION: - Norfolk and Norwich University Hospital, Norwich, UK, f.carey@uea.ac.uk.

RESUMEN / SUMMARY: - INTRODUCTION: There are plausible biological mechanisms for how statins may prevent pancreatic cancer, although the evidence from epidemiological studies in the general population is conflicting. This study aims to clarify whether statins exert their effects in specific sub-

groups, namely, gender, smoking status and diabetes. METHODS: A matched case-control study was conducted in patients diagnosed with pancreatic cancer, and a group of dermatology patients of similar ages and gender, diagnosed with basal cell carcinoma. Participants' medical records were reviewed for information on statin use prior to diagnosis. Odds ratios and 95 % CIs for the development of pancreatic cancer were estimated using conditional logistic regression. Subgroup analysis was performed in men, women, smokers and those with type 2 diabetes. RESULTS: Two hundred fifty-two cases (median age 71 years, range 48-73 years, 51 % women) and 504 controls were identified, of which 23 % of cases were regular statin users versus 21 % of controls. In the general study population there was no association between pancreatic cancer and regular statin use (OR 0.82, 95 % CI 0.53-1.23, p = 0.33). However, in male smokers, regular statin use was associated with significantly reduced odds of pancreatic cancer compared to male smokers not prescribed a statin (OR 0.11, 95 % CI 0.01-0.96, p = 0.05). In patients with type 2 diabetes statins use was not associated with reduced odds (OR 0.92, 95 % CI 0.35-2.45, p = 0.80), with no gender effects. CONCLUSIONS: In male smokers, statins may reduce the odds of pancreatic cancer. Statin use should be measured in aetiological studies of pancreatic cancer but analysed in specific sub-groups. Future work should investigate statins as chemopreventative agents in this high risk sub-group.

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[115]

TÍTULO / TITLE: - Sensitization of Pancreatic Cancer to Chemoradiation by the Chk1 Inhibitor MK8776.

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

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Jul 25.

●● Enlace al texto completo (gratuito o de pago) 1158/1078-0432.CCR-12-3748

AUTORES / AUTHORS: - Engelke CG; Parsels LA; Qian Y; Zhang Q; Karnak D; Robertson JR; Tanska DM; Wei D; Davis MA; Parsels JD; Zhao L; Greenson JK; Lawrence TS; Maybaum J; Morgan MA

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of Radiation Oncology, Pharmacology, and Pathology, University of Michigan Medical School; and Biostatistics Unit, University of Michigan Comprehensive Cancer Center, Ann Arbor, Michigan.

RESUMEN / SUMMARY: - PURPOSE: The combination of radiation with chemotherapy is the most effective therapy for unresectable pancreatic cancer. To improve upon this regimen, we combined the selective Checkpoint kinase 1 (Chk1) inhibitor MK8776 with gemcitabine-based chemoradiation in preclinical pancreatic cancer models.EXPERIMENTAL DESIGN: We tested the ability of MK8776 to sensitize to gemcitabine-radiation in homologous recombination repair (HRR)-proficient and -deficient pancreatic cancer cells and assessed

Rad51 focus formation. In vivo, we investigated the efficacy, tumor cell selectivity, and pharmacodynamic biomarkers of sensitization by MK8776.RESULTS: We found that MK8776 significantly sensitized HRR-proficient (AsPC-1, MiaPaCa-2, BxPC-3) but not -deficient (Capan-1) pancreatic cancer cells to gemcitabine-radiation and inhibited Rad51 focus formation in HRR-proficient cells. In vivo, MiaPaCa-2 xenografts were significantly sensitized to gemcitabine-radiation by MK8776 without significant weight loss or observable toxicity in the small intestine, the dose-limiting organ for chemoradiation therapy in pancreatic cancer. We also assessed pChk1 (S345), a pharmacodynamic biomarker of DNA damage in response to Chk1 inhibition in both tumor and small intestine and found that MK8776 combined with gemcitabine or gemcitabine-radiation produced a significantly greater increase in pChk1 (S345) in tumor relative to small intestine, suggesting greater DNA damage in tumor than in normal tissue. Furthermore, we demonstrated the utility of an ex vivo platform for assessment of pharmacodynamic biomarkers of Chk1 inhibition in pancreatic cancer.CONCLUSIONS: Together, our results suggest that MK8776 selectively sensitizes HRR-proficient pancreatic cancer cells and xenografts to gemcitabine-radiation and support the clinical investigation of MK8776 in combination with gemcitabine-radiation in locally advanced pancreatic cancer. Clin Cancer Res; 1-10. ©2013 AACR.

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[116]

TÍTULO / TITLE: - Association of XRCC1 gene single nucleotide polymorphisms and susceptibility to pancreatic cancer in Chinese.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Jul 27.

●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-1001-y

AUTORES / AUTHORS: - Chen H; Tang C; Liu M; Zhou B; Kuang Y; 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 human X-ray repair cross-complementing group 1 gene (XRCC1) is an important candidate gene for affecting pancreatic cancer (PC) risk. The objective of this study was to detect whether the c.1471G > A and c.1686C > G polymorphisms of XRCC1 gene influence PC risk. The association of XRCC1 genetic variants with PC risk was analyzed in 328 PC patients and 350 controls by the polymerase chain reaction-restriction fragment length polymorphism and created restriction site-polymerase chain reaction method. Our data suggested that the genotypes and alleles from these two genetic variants were statistically associated with PC risk. For c.1471G > A, the AA genotype was associated with the decreased risk of developing PC

compared to GG wild genotype (odds ratio (OR) = 0.43, 95 % confidence intervals (CI) 0.26-0.70, chi-squared (chi 2) = 11.91, P = 0.001). For c.1686C > G, the risk of PC was significantly lower for GG genotype in comparing to CC wild genotype (OR = 0.48, 95 % CI 0.29-0.81, chi 2 = 7.98, P = 0.005). The A allele of c.1471G > A and G allele of c.1686C > G genetic variants could contribute to decrease the risk of PC (for c.1471G > A: A vs G, OR = 0.65, 95 % CI 0.52-0.82, chi 2 = 13.71, P < 0.001, for c.1686C > G: G vs C, OR = 0.70, 95 % CI 0.55-0.88, chi 2 = 9.42, P = 0.002). Our findings indicate that the c.1471G > A and c.1686C > G polymorphisms of XRCC1 gene are associated with PC risk in Chinese population.

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[117]

TÍTULO / TITLE: - Integrated Genomic, Transcriptomic, and RNA-Interference Analysis of Genes in Somatic Copy Number Gains in Pancreatic Ductal Adenocarcinoma.

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

REVISTA / JOURNAL: - Pancreas. 2013 Aug;42(6):1016-26. doi: 10.1097/MPA.0b013e318287d043.

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

1097/MPA.0b013e318287d043

AUTORES / AUTHORS: - Samuel N; Sayad A; Wilson G; Lemire M; Brown KR; Muthuswamy L; Hudson TJ; Moffat J

INSTITUCIÓN / INSTITUTION: - From the *Department of Molecular Genetics, University of Toronto; daggerOntario Institute for Cancer Research; double daggerOntario Cancer Institute, University Health Network; and section signDonnelly Centre and Banting & Best Department of Medical Research, and parallelDepartment of Medical Biophysics, University of Toronto, Toronto, Ontario, Canada.

RESUMEN / SUMMARY: - OBJECTIVES: This study used an integrated analysis of copy number, gene expression, and RNA interference screens for identification of putative driver genes harbored in somatic copy number gains in pancreatic ductal adenocarcinoma (PDAC). METHODS: Somatic copy number gain data on 60 PDAC genomes were extracted from public data sets to identify genomic loci that are recurrently gained. Array-based data from a panel of 29 human PDAC cell lines were used to quantify associations between copy number and gene expression for the set of genes found in somatic copy number gains. The most highly correlated genes were assessed in a compendium of pooled short hairpin RNA screens on 27 of the same human PDAC cell lines. RESULTS: A catalog of 710 protein-coding and 46 RNA genes mapping to 20 recurrently gained genomic loci were identified. The gene set was further refined through stringent integration of copy number, gene expression, and RNA interference screening data to uncover 34 candidate driver genes. CONCLUSIONS: Among the candidate genes from the integrative analysis,

ECT2 was found to have significantly higher essentiality in specific PDAC cell lines with genomic gains at the 3q26.3 locus, which harbors this gene, suggesting that ECT2 may play an oncogenic role in the PDAC neoplastic process.

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[118]

TÍTULO / TITLE: - Clinical significance of RECK promoter methylation in pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Jun 8.

●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-0903-z

AUTORES / AUTHORS: - Lu XX; Zhang SM; Fang Y; Wang ZT; Xie JJ; Zhan Q; Deng XX; Chen H; Jin JB; Peng CH; Li HW; Shen BY

INSTITUCIÓN / INSTITUTION: - Center of Organ Transplantation, Ruijin Hospital, School of Medicine, Shanghai Jiaotong University, No. 197, Ruijiner Road, Shanghai, 200025, China.

RESUMEN / SUMMARY: - The aim of this study was to analyze the clinical significance of reversion-inducing-cysteine-rich protein with Kazal motifs (RECK) promoter methylation in pancreatic ductal adenocarcinoma (PDA). Methylation-specific polymerase chain reaction was used to examine the promoter methylation status of RECK in 60 pairs of PDA tissue samples and adjacent non-cancerous tissue samples. Statistical analyses were applied to test the associations between RECK promoter methylation status, clinicopathologic factors, and prognosis. The rate of RECK promoter methylation was significantly higher in PDA tissues than in adjacent non-cancerous tissues ($P < 0.001$). RECK methylation status was significantly associated with clinical stage ($P = 0.017$), histological differentiation ($P = 0.046$), and lymph node metastasis ($P = 0.003$), but was not associated with gender, age, and tumor location (all $P > 0.05$). Additionally, RECK promoter methylation is associated with malignant behavior and poor prognosis. In conclusion, determination of RECK promoter methylation status in tumor tissues may assist in the identification of patients who require aggressive postoperative intervention in order to improve prognosis.

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[119]

TÍTULO / TITLE: - The discrete nature and distinguishing molecular features of pancreatic intraductal tubulopapillary neoplasms and intraductal papillary mucinous neoplasms of the gastric type, pyloric gland variant.

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

REVISTA / JOURNAL: - J Pathol. 2013 Jul 25. doi: 10.1002/path.4242.

●● Enlace al texto completo (gratuito o de pago) 1002/path.4242

AUTORES / AUTHORS: - Yamaguchi H; Kuboki Y; Hatori T; Yamamoto M; Shimizu K; Shiratori K; Shibata N; Shimizu M; Furukawa T

INSTITUCIÓN / INSTITUTION: - Institute for Integrated Medical Sciences, Tokyo Women's Medical University, Tokyo, Japan; Department of Pathology, Saitama International Medical Center, Saitama Medical University, Hidaka, Japan.

RESUMEN / SUMMARY: - Intraductal tubulopapillary neoplasms (ITPNs) are composed of tubulopapillary glands with high-grade dysplasia in the pancreatic duct. Intraductal papillary mucinous neoplasms of the gastric type, pyloric gland variant (IPMN-PGs) are composed of tubular glands mimicking pyloric glands with low-grade dysplasia, which was formerly called intraductal tubular adenoma. Because of their apparent common tubular morphology, IPMN-PG and ITPN could be associated. While the former might progress to the latter, this has not been fully assessed. In this study, we compared molecular features of ITPNs and IPMN-PGs to determine their association using formalin-fixed, paraffin-embedded tissues of 14 ITPNs and 15 IPMN-PGs. Somatic mutations in PIK3CA, GNAS, KRAS, and BRAF were determined by Sanger sequencing. Expression of phosphorylated AKT was examined by immunohistochemistry. Somatic PIK3CA mutations were found in 3 of 14 ITPNs (21.4%) but in none of the IPMN-PGs ($p = 0.0996$). In contrast, GNAS mutations were found in none of the ITPNs but in 9 of 15 IPMN-PGs (60.0%; $p < 0.001$). KRAS mutations were detected in 1 of 14 ITPNs (7.1%) and 12 of 15 IPMN-PGs (80.0%; $p < 0.001$). BRAF mutation was found in 1 ITPN but in none of the IPMN-PGs. Phosphorylated AKT expression in ITPNs was significantly more evident than that in IPMN-PGs ($p = 0.0401$). These results indicate that ITPNs and IPMN-PGs are molecularly distinct, suggesting that IPMN-PG does not progress to ITPN. Furthermore, the molecular features of IPMN-PGs are confirmed to be identical to those of IPMNs reported elsewhere. These results validate the current World Health Organization system that classifies pancreatic intraductal neoplasms into IPMN and ITPN and confirm that IPMN-PG is not a benign counterpart of ITPN. The term "intraductal tubular adenoma" should be eliminated and replaced with IPMN-PG.

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[120]

TÍTULO / TITLE: - Clinical significance of serum M30 and M65 levels in metastatic pancreatic adenocarcinoma.

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

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

●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-0931-8

AUTORES / AUTHORS: - Tas F; Karabulut S; Bilgin E; Sen F; Yildiz I; Tastekin D; Ciftci R; Duranyildiz D

INSTITUCIÓN / INSTITUTION: - Institute of Oncology, University of Istanbul, Capa, 34390, Istanbul, Turkey, faruktas2002@yahoo.com.

RESUMEN / SUMMARY: - M30 and M65 are relatively new assays that detect different circulating forms of the epithelial cell structural protein cytokeratin 18. This study was conducted to investigate the serum levels of M30 and M65 in patients with metastatic pancreatic adenocarcinoma (MPA) and the relationship with tumor progression and known prognostic parameters. Twenty-six patients with MPA were investigated. Serum samples were obtained on first admission before treatment and follow-up. Both serum M30 and M65 levels were determined using enzyme-linked immunosorbent assay. The median age at diagnosis was 59 years, range 32-80 years; 14 patients were men. All patients had metastatic stage, and most (n = 21, 81 %) had hepatic metastasis. The baseline levels of both serum M30 and serum M65 were significantly higher in patients with MPA than those in the control group ($p < 0.001$, for both assays). Serum M65 level was only significantly higher in the patients with elevated serum LDH levels than in others with normal serum LDH levels ($p = 0.03$). For serum M30 levels, no correlation was found. The significant relationship was found between the serum levels of M30 and M65 ($r s = 0. 926$, $n = 26$, $p < 0.001$, Spearman's correlation). The median survival for all patients was 31.7 +/- 2.2 weeks (95 % CI = 27.31-36.08). Although only the serum LDH level was found to be a significant prognostic factor ($p = 0.01$), neither serum M30 nor serum M65 had significant effect on survival ($p = 0.28$ and $p = 0.15$, respectively). In conclusion, although both serum levels of M30 and M65 assays were found to be of diagnostic value, no predictive and prognostic values were determined in MPA patients.

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[121]

TÍTULO / TITLE: - Epithelial-mesenchymal transition markers in the differential diagnosis of gastroenteropancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - Am J Clin Pathol. 2013 Jul;140(1):61-72. doi: 10.1309/AJCPIV40ISTBXRAX.

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

1309/AJCPIV40ISTBXRAX

AUTORES / AUTHORS: - Galvan JA; Astudillo A; Vallina A; Fonseca PJ; Gomez-Izquierdo L; Garcia-Carbonero R; Gonzalez MV

INSTITUCIÓN / INSTITUTION: - Laboratorio del Banco de Tumores-Anatomia Patologica, c/ Celestino Villamil, s/n, 33006 Oviedo, España. galvanjose@uniovi.es

RESUMEN / SUMMARY: - OBJECTIVES: To elucidate the role of epithelial-mesenchymal transition markers in gastroenteropancreatic neuroendocrine tumors (GEP NETs) and the potential usefulness in their clinical management. METHODS: One hundred ten GEP NET paraffin-embedded samples were immunohistochemically analyzed for E-cadherin, N-cadherin, beta-catenin, vimentin, Snail1, Snail2, Twist, and Foxc2 protein expression. RESULTS: The

5-year survival rate was reduced for those patients showing high Snail1 protein levels, a cytoplasmic E-cadherin pattern, reduced N-cadherin expression, and loss of E-cadherin/beta-catenin adhesion complex integrity at the cell membrane. Interestingly, high beta-catenin expression was useful in identifying a grade 1 NET subgroup with a favorable clinical course. Importantly, it also helped to discriminate small-cell vs large-cell grade 3 neuroendocrine carcinomas. CONCLUSIONS: beta-Catenin and N-cadherin immunohistochemical detection might be a useful tool in the differential diagnosis of small-cell vs large-cell G3 neuroendocrine carcinomas. High Snail1 and Foxc2 expression is associated with the invasion and metastatic spread of GEP NETs.

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[122]

TÍTULO / TITLE: - Comparative benefits of Nab-paclitaxel over gemcitabine or polysorbate-based docetaxel in experimental pancreatic cancer.

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

REVISTA / JOURNAL: - Carcinogenesis. 2013 Aug 2.

●● Enlace al texto completo (gratuito o de pago) 1093/carcin/bgt227

AUTORES / AUTHORS: - Awasthi N; Zhang C; Schwarz AM; Hinz S; Wang C; Williams NS; Schwarz MA; Schwarz RE

INSTITUCIÓN / INSTITUTION: - Division of Surgical Oncology, Department of Surgery.

RESUMEN / SUMMARY: - Gemcitabine has limited clinical benefits in pancreatic ductal adenocarcinoma. The solvent-based traditional taxanes docetaxel and paclitaxel have not shown clinical results superior to gemcitabine. Nab-paclitaxel, a water-soluble albumin-bound paclitaxel, may carry superior distribution properties into the tumor microenvironment and has shown efficacy in multiple tumor types. We evaluated nab-paclitaxel effects compared with gemcitabine or docetaxel. For pancreatic ductal adenocarcinoma cells AsPC-1, BxPC-3, MIA PaCa-2 and Panc-1, gemcitabine IC50 ranged from 494nM to 23.9 muM; docetaxel IC50 range was from 5 to 34nM; nab-paclitaxel IC50 range was from 243nM to 4.9 muM. Addition of IC25 dose of docetaxel or nab-paclitaxel decreased gemcitabine IC50. Net tumor growth inhibition after gemcitabine, docetaxel or nab-paclitaxel was 67, 31 and 72%, which corresponded with intratumoral proliferative and apoptotic indices. Tumor stromal density was decreased by nab-paclitaxel and to a lesser extent by docetaxel as measured through reduction in alpha-smooth muscle actin, S100A4 and collagen 1 expression. Animal survival was prolonged after nab-paclitaxel treatment (41 days, $P < 0.002$) compared with gemcitabine (32 days, $P = 0.005$), docetaxel (32 days, $P = 0.005$) and controls (20 days). Survival in nab-paclitaxel/gemcitabine and docetaxel/gemcitabine sequential treatment groups was not superior to nab-paclitaxel alone. Low-dose combination of gemcitabine with nab-paclitaxel or docetaxel was more effective compared with

controls or gemcitabine alone but not superior to regular dose nab-paclitaxel alone. Combination treatment of gemcitabine+nab-paclitaxel or gemcitabine+docetaxel increased gemcitabine concentration in plasma and tumor. The superior antitumor activity of nab-paclitaxel provides a strong rationale for considering nab-paclitaxel as first-line monotherapy in pancreatic ductal adenocarcinoma.

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[123]

TÍTULO / TITLE: - Inhibitory effect of geraniol in combination with gemcitabine on proliferation of BXPC-3 human pancreatic cancer cells.

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

REVISTA / JOURNAL: - J Int Med Res. 2013 Aug;41(4):993-1001. doi: 10.1177/0300060513480919. Epub 2013 Jun 25.

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

1177/0300060513480919

AUTORES / AUTHORS: - Jin X; Sun J; Miao X; Liu G; Zhong D

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The Second Xiangya Hospital, Central South University, Changsha, Hunan Province, China.

RESUMEN / SUMMARY: - OBJECTIVE: To investigate the inhibitory effect of geraniol alone, or in combination with gemcitabine, on the proliferation of BXPC-3 pancreatic cancer cells. METHODS: BXPC-3 cells were treated under different conditions: with geraniol at 10, 20, 40, 80 and 160 micromol/l each for 24 h, 48 h or 72 h; with 20 micromol/l geraniol for 24 h or 0 h before 20 micromol/l gemcitabine for 24 h; with 20 micromol/l geraniol for 24 h, 48 h and 72 h following 20 micromol/l gemcitabine for 24 h; or with 20 micromol/l gemcitabine alone as a control. Cell proliferation was assessed and changes in cell morphology were assessed by light and fluorescence microscopy. Apoptosis was detected using flow cytometry. RESULTS: Geraniol inhibited BXPC-3 cell proliferation in a time- and dosa-dependent manner. Geraniol alone or combined with gemcitabine induced BXPC-3 cell apoptosis. BXPC-3 inhibition rates with combined treatment were 55.24%, 50.69%, 49.83%, 41.85% and 45.27% following treatment with 20 micromol/l geraniol for 24 h or 0 h before 20 micromol/l gemcitabine for 24 h, or 20 micromol/l geraniol for 24 h, 48 h and 72 h, following 20 micromol/l gemcitabine for 24 h, respectively. CONCLUSION: Geraniol inhibited the proliferation of BXPC-3 cells. Geraniol significantly increased the antiproliferative and apoptosis-inducing effects of gemcitabine on BXPC-3 cells. Maximum inhibition of BXPC-3 cells was achieved with geraniol treatment for 24 h before gemcitabine treatment.

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[124]

TÍTULO / TITLE: - Nuclear Expression of Glioma-Associated Oncogene Homolog 1 and Nuclear Factor-kappaB Is Associated with a Poor Prognosis of Pancreatic Cancer.

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

REVISTA / JOURNAL: - Oncology. 2013 Jul 16;85(2):86-94.

●● Enlace al texto completo (gratuito o de pago) 1159/000353452

AUTORES / AUTHORS: - Yang SH; Hsu CH; Lee JC; Tien YW; Kuo SH; Cheng AL

INSTITUCIÓN / INSTITUTION: - Department of Oncology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan.

RESUMEN / SUMMARY: - Objective: We investigated the association of the hedgehog pathway with nuclear factor (NF)-kappaB and clinical outcomes in pancreatic cancer patients. Methods: We analyzed tissue samples for the expression of NF-kappaB (RelA/p65), sonic hedgehog (Shh) and glioma-associated oncogene homolog 1 (Gli1) by immunohistochemistry and investigated their expression in association with clinical outcomes. Results: Eighty-one patients with pancreatic cancer were investigated. Expression of Shh and nuclear expression of Gli1 and NF-kappaB were found in 63 of 66 (96%), 28 of 68 (41%) and 22 of 68 cases (32%), respectively. Nuclear Gli1 expression was closely associated with nuclear expression of NF-kappaB ($p < 0.001$). Patients with nuclear Gli1 had significantly worse prognoses than those without (median survival 7.9 vs. 13.9 months; $p = 0.009$). Similarly, patients with nuclear expression of NF-kappaB had shorter overall survival than those with negative or cytoplasmic expression of NF-kappaB (median survival 5.5 vs. 13.9 months; $p < 0.001$). Shh expression had no prognostic significance. In the multivariate analysis, NF-kappaB nuclear expression was closely associated with unfavorable overall survival ($p = 0.02$). Conclusion: Our results indicate that nuclear expression of Gli1 or NF-kappaB is a strong predictor of poor prognosis in pancreatic cancer. Additional investigation of the biologic significance of this association is warranted. © 2013 S. Karger AG, Basel.

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[125]

TÍTULO / TITLE: - Interfractional position variation of pancreatic tumors quantified using intratumoral fiducial markers and daily cone beam computed tomography.

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

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Sep 1;87(1):202-8. doi: 10.1016/j.ijrobp.2013.05.001. Epub 2013 Jun 19.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ijrobp.2013.05.001

AUTORES / AUTHORS: - van der Horst A; Wognum S; Davila Fajardo R; de Jong R; van Hooft JE; Fockens P; van Tienhoven G; Bel A

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands. Electronic address: a.vanderhorst@amc.uva.nl.

RESUMEN / SUMMARY: - PURPOSE: The aim of this study was to quantify interfractional pancreatic position variation using fiducial markers visible on daily cone beam computed tomography (CBCT) scans. In addition, we analyzed possible migration of the markers to investigate their suitability for tumor localization. METHODS AND MATERIALS: For 13 pancreatic cancer patients with implanted Visicoil markers, CBCT scans were obtained before 17 to 25 fractions (300 CBCTs in total). Image registration with the reference CT was used to determine the displacement of the 2 to 3 markers relative to bony anatomy and to each other. We analyzed the distance between marker pairs as a function of time to identify marker registration error (SD of linear fit residuals) and possible marker migration. For each patient, we determined the mean displacement of markers relative to the reference CT (systematic position error) and the spread in displacements (random position error). From this, we calculated the group systematic error, Sigma, and group random error, sigma. RESULTS: Marker pair distances showed slight trends with time (range, -0.14 to 0.14 mm/day), possibly due to tissue deformation, but no shifts that would indicate marker migration. The mean SD of the fit residuals was 0.8 mm. We found large interfractional position variations, with for 116 of 300 (39%) fractions a 3-dimensional vector displacement of >10 mm. The spread in displacement varied significantly (P<.01) between patients, from a vector range of 9.1 mm to one of 24.6 mm. For the patient group, Sigma was 3.8, 6.6, and 3.5 mm; and sigma was 3.6, 4.7 and 2.5 mm, in left-right, superior-inferior, and anterior-posterior directions, respectively. CONCLUSIONS: We found large systematic displacements of the fiducial markers relative to bony anatomy, in addition to wide distributions of displacement. These results for interfractional position variation confirm the potential benefit of using fiducial markers rather than bony anatomy for daily online position verification for pancreatic cancer patients.

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[126]

TÍTULO / TITLE: - Structure-activity relationship (SAR) of withanolides to inhibit Hsp90 for its activity in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Invest New Drugs. 2013 Jul 26.

●● Enlace al texto completo (gratuito o de pago) 1007/s10637-013-9987-y

AUTORES / AUTHORS: - Gu M; Yu Y; Gunaherath GM; Gunatilaka AA; Li D; Sun D

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical Sciences, College of Pharmacy, The University of Michigan, 428 Church Street, Ann Arbor, MI, 48109, USA.

RESUMEN / SUMMARY: - Withaferin A (WA), a naturally occurring steroidal lactone, directly binds to Hsp90 and leads to the degradation of Hsp90 client protein. The purpose of this study is to investigate the structure activity relationship (SAR) of withanolides for their inhibition of Hsp90 and anti-proliferative activities in pancreatic cancer cells. In pancreatic cancer Panc-1 cells, withaferin A (WA) and its four analogues withanolide E (WE), 4-hydroxywithanolide E (HWE), 3-aziridinylwithaferin A (AzWA) inhibited cell proliferation with IC50 ranged from 1.0 to 2.8 muM. WA, WE, HWE, and AzWA also induced caspase-3 activity by 21-, 6-, 11- and 15-fold, respectively, in Panc-1 cells, while withaperuvin (WP) did not show any activity. Our data showed that WA, WE, HWE, and AzWA, but not WP, all directly bound to Hsp90 and induced Hsp90 aggregation,hence inhibited Hsp90 chaperone activity to induce degradation of Hsp90 client proteins Akt and Cdk4 through proteasome-dependent pathway in pancreatic cancer cells. However, only WA, HWE and AzWA disrupted Hsp90-Cdc37 complexes but not WE and WP. SAR study suggested that the C-5(6)-epoxy functional group contributes considerably for withanolide to bind to Hsp90, inhibit Hsp90 chaperone activity, and result in Hsp90 client protein depletion. Meanwhile, the hydroxyl group at C-4 of ring A may enhance withanolide to inhibit Hsp90 activity and disrupt Hsp90-Cdc37 interaction. These SAR data provide possible mechanisms of anti-proliferative action of withanolides.

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[127]

TÍTULO / TITLE: - Population-Level Analysis of Pancreatic Neuroendocrine Tumors 2 cm or Less in Size.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Sep;20(9):2815-21. doi: 10.1245/s10434-013-3005-7. Epub 2013 Jun 15.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3005-7

AUTORES / AUTHORS: - Kuo EJ; Salem RR

INSTITUCIÓN / INSTITUTION: - Section of Surgical Oncology, Department of Surgery, Yale University School of Medicine, New Haven, CT, USA.

RESUMEN / SUMMARY: - BACKGROUND: There is a paucity of evidence regarding incidence and predictors of survival in pancreatic neuroendocrine tumors (PNETs) </=2 cm in size. METHODS: Patients having undergone resection for nonfunctioning PNETs were selected from the SEER database (1988-2009) and an institutional pathology database (1996-2012). PNETs </=2 cm were compared with PNETs >2 cm. Data were analyzed with chi (2) tests, ANOVA, the Kaplan-Meier method, log rank tests, and Cox proportional hazard, and binary logistic regression. RESULTS: The incidence of PNETs </=2 cm in the United States has increased by 710.4 % over the last 22 years. Rates of extrapancreatic extension, nodal metastasis, and distant metastasis in PNETs

</=2 cm in the SEER database were 17.9, 27.3, and 9.1 %, respectively. The rate of nodal metastasis in our institutional series was 5.7 %. Disease-specific survival at 5, 10, and 15 years for PNETs </=2 cm was 91.5, 84.0, and 76.8 %. Decreased disease-specific survival was not associated with nodal metastasis, but rather with high grade [moderately differentiated, hazard ratio (HR) 37.2, 95 % confidence interval (CI) 2.7-518.8; poorly differentiated, HR 94.2, 95 % CI 4.9-1,794.4; reference, well differentiated], and minority race (Asian, HR 30.2, 95 % CI 3.1-291.7; Black, HR 60.1, 95 % CI 2.1-1,027.9; reference, White). CONCLUSIONS: Pancreatic neuroendocrine tumors </=2 cm are increasingly common, and the most significant predictors of disease-specific survival are grade and race. The SEER database excludes PNETs considered to be benign, and rates of extrapancreatic extension, nodal metastasis, and distant metastasis are overestimated. Small size, however, does not preclude malignant behavior.

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[128]

TÍTULO / TITLE: - Clinical Utility of Endoscopic Ultrasound Elastography for Identification of Malignant Pancreatic Masses: A Meta-Analysis.

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

REVISTA / JOURNAL: - J Gastroenterol Hepatol. 2013 Jun 4. doi: 10.1111/jgh.12292.

●● Enlace al texto completo (gratuito o de pago) 1111/jgh.12292

AUTORES / AUTHORS: - Ying L; Lin X; Xie ZL; Hu YP; Tang KF; Shi KQ

INSTITUCIÓN / INSTITUTION: - Department of Ultrasonography, the First Affiliated Hospital of Wenzhou Medical College, Wenzhou 325000, China.

RESUMEN / SUMMARY: - BACKGROUND AND AIM: Endoscopic ultrasound (EUS) elastography is not used for detection, but rather for characterization of solid pancreatic masses. A meta-analysis was used to assess the accuracy of EUS elastography for identification of malignant pancreatic masses. METHODS: PubMed, the Cochrane Library, and the ISI web of Knowledge were searched. The studies relating to evaluation accuracy of qualitative or quantitative EUS elastography for identification of malignant pancreatic masses were collected. Language was limited to English. The sensitivity and specificity were used to examine the accuracy. Clinical utility was evaluated by likelihood ratio (LR) scattergram. RESULTS: A total of 10 studies including 893 pancreatic masses (646 malignant, 72.3%) were analyzed. The summary sensitivity and specificity for the diagnosis of malignant pancreatic masses were 0.98 (95% confidence interval (CI), 0.93-1.00) and 0.69 (95% CI, 0.52-0.82) for qualitative EUS elastography, and 0.96 (95% CI, 0.86-0.99) and 0.76 (95% CI, 0.58-0.87) for quantitative EUS elastography, respectively. The hierarchical summary receiver operating characteristic curves were 0.94 and 0.93 for qualitative and quantitative EUS elastography. The accuracy of quantitative methods was similar to qualitative methods. The positive and negative LRs were 3.15 and

0.03 for qualitative EUS elastography, and 3.94 and 0.05 for quantitative EUS elastography, respectively. Both qualitative and quantitative methods were useful for exclusion of presence of malignant pancreatic masses and not for its confirmation. CONCLUSIONS: EUS elastography could be used as a good identification tool for benign and malignant pancreatic masses, with its good performance for exclusion of presence of malignant pancreatic masses.

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[129]

TÍTULO / TITLE: - Alternatively spliced tissue factor contributes to tumor spread and activation of coagulation in pancreatic ductal adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Int J Cancer. 2013 Jun 10. doi: 10.1002/ijc.28327.
●● Enlace al texto completo (gratuito o de pago) 1002/ijc.28327
AUTORES / AUTHORS: - Unruh D; Turner K; Srinivasan R; Kocaturk B; Qi X; Chu Z; Aronow BJ; Plas DR; Gallo CA; Kalthoff H; Kirchhofer D; Ruf W; Ahmad SA; Lucas FV; Versteeg HH; Bogdanov VY
INSTITUCIÓN / INSTITUTION: - Division of Hematology/Oncology, Internal Medicine, University of Cincinnati College of Medicine, Cincinnati, OH.
RESUMEN / SUMMARY: - Alternatively spliced tissue factor (asTF) promotes neovascularization and monocyte recruitment via integrin ligation. While asTF mRNA has been detected in some pancreatic ductal adenocarcinoma (PDAC) cell lines and increased asTF expression can promote PDAC growth in a subcutaneous model, the expression of asTF protein in bona fide PDAC lesions and/or its role in metastatic spread are yet to be ascertained. We here report that asTF protein is abundant in lesional and stromal compartments of the five studied types of carcinoma including PDAC. Analysis of 29 specimens of PDAC revealed detectable asTF in >90% of the lesions with a range of staining intensities. asTF levels in PDAC lesions positively correlated with the degree of monocyte infiltration. In an orthotopic model, asTF-overexpressing high-grade PDAC cell line Pt45P1/asTF+ produced metastases to distal lymph nodes, which stained positive for asTF. PDAC cells stimulated with and/or overexpressing asTF exhibited upregulation of genes implicated in PDAC progression and metastatic spread. Pt45P1/asTF+ cells displayed higher coagulant activity compared to Pt45P1 cells; the same effect was observed for cell-derived microparticles (MPs). Our findings demonstrate that asTF is expressed in PDAC and lymph node metastases and potentiates PDAC spread in vivo. asTF elicits global changes in gene expression likely involved in tumor progression and metastatic dissemination, and it also enhances the procoagulant potential of PDAC cells and cell-derived MPs. Thus, asTF may comprise a novel therapeutic target to treat PDAC and, possibly, its thrombotic complications.

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[130]

TÍTULO / TITLE: - Pancreatic panniculitis secondary to acinar cell carcinoma of the pancreas.

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

REVISTA / JOURNAL: - Cutis. 2013 Apr;91(4):186-90.

AUTORES / AUTHORS: - Gorovoy IR; McSorley J; Gorovoy JB

INSTITUCIÓN / INSTITUTION: - Department of Ophthalmology, University of Califomia, San Francisco, USA. gorovoyi@vision.ucsf.edu

RESUMEN / SUMMARY: - We report the case of a 68-year-old white woman who presented with painful, 1- to 4-cm, erythematous nodules located bilaterally on the anterior and medial shins that had progressively developed and worsened over the last month. Workup revealed pancreatic panniculitis (PP) secondary to acinar cell carcinoma of the pancreas (ACCP). The unique clinicopathologic features, differential diagnosis, underlying causes, associated laboratory and clinical findings, pathophysiology, treatments, and appropriate workup for PP also are reviewed.

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[131]

TÍTULO / TITLE: - KRAS mutational analysis and immunohistochemical studies can help distinguish pancreatic metastases from primary lung adenocarcinomas.

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

REVISTA / JOURNAL: - Mod Pathol. 2013 Jul 26. doi: 10.1038/modpathol.2013.146.

●● Enlace al texto completo (gratuito o de pago)
1038/modpathol.2013.146

AUTORES / AUTHORS: - Krasinskas AM; Chiosea SI; Pal T; Dacic S

INSTITUCIÓN / INSTITUTION: - Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.

RESUMEN / SUMMARY: - Lung metastases from primary pancreatic adenocarcinomas often have mucinous features, which makes them difficult to distinguish from the primary lung adenocarcinoma. We explored the potential utility of KRAS mutational status and immunohistochemical studies in the evaluation of adenocarcinomas in the lungs of patients with known pancreatic cancer. Metastatic pancreatic cancer cases had fewer solitary lung lesions (5 (15%) versus 37 (95%) for lung primaries; P=0.0001), more tumors with pure (100%) mucinous morphology (16 (50%) versus 9 (23%) for lung primaries; P=0.0037), and more frequent KRAS mutations (24 (75%) versus 18 (46%) for lung primaries; P=0.0093). Presence of the KRAS G12C mutation had 96% specificity and positive predictive value for lung adenocarcinoma, whereas G12R was 99% specific for pancreatic cancer with a positive predictive value of 86%. Of the 18 KRAS mutated mucinous lung tumors, only 3 (16%) occurred in

nonsmokers. Conversely, of the 19 KRAS mutated pancreatic cancer metastases, 11 (58%) occurred in nonsmokers. The median overall survival was significantly shorter for patients with metastatic tumors when compared with patients with primary mucinous tumors (19 months, 95% confidence interval, 10-28 months versus 55 months, 95% confidence interval, 39-70 months, P=0.005). CK20 and CDX2 positivity supported metastatic pancreatic cancer, whereas TTF-1 positivity supported primary lung adenocarcinoma. In summary, KRAS G12C mutations, TTF-1, and napsin A were associated with primary lung adenocarcinoma, whereas KRAS G12R mutations, CK20, and CDX2 favored pancreatic adenocarcinoma. We showed survival differences for patients whose pancreatic metastases were synchronous versus metachronous to their primary tumors, and for patients with mucinous pancreatic cancer metastases versus primary mucinous lung adenocarcinomas. Differences in KRAS mutations reflect differences in exposure to tobacco smoking and highlight biological differences between two KRAS oncogene-driven cancers.Modern Pathology advance online publication, 26 July 2013; doi:10.1038/modpathol.2013.146.

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[132]

TÍTULO / TITLE: - Folfox4 as a rescue chemotherapy for gemcitabine-refractory pancreatic cancer.

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

REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Mar-Apr;60(122):363-7.

AUTORES / AUTHORS: - Chung JW; Jang HW; Chung MJ; Park JY; Park SW; Chung JB; Song SY; Bang S

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Yonsei Institute of Gastroenterology, Seoul, Korea.

RESUMEN / SUMMARY: - BACKGROUND/AIMS: This phase II study assessed the efficacy and safety of FOLFOX4 as a rescue therapy in patients with gemcitabine-refractory pancreatic cancer. METHODOLOGY: The study included patients with advanced pancreatic cancer who had failed gemcitabine-based chemotherapy. FOLFOX4 was administered biweekly as follows: oxaliplatin, 85 mg/m(2) as a 2-hour infusion (day 1); leucovorin, 200 mg/m(2)/day as a 2-hour infusion (days 1 and 2); 5-fluorouracil, bolus 400 mg/m(2)/day and 600 mg/m(2)/day as a 22-hour infusion (days 1 and 2). RESULTS: Forty-four patients received a total of 264 cycles of chemotherapy. There was 1 complete response (2.2%), 4 partial responses (9.1%), and 13 stable diseases (29.5%). The objective response rate was 11.4% and the tumor stabilization rate was 40.9%. The median time to progression was 9.9 weeks (95%CI: 8.2-11.5) and the median overall survival was 31.1 weeks (95%CI: 24.4-37.9). The common adverse events were hematologic toxicities: grade 3 or 4 neutropenia in 19 patients (43.2%), anemia in 9 patients (20.5%), and thrombocytopenia in 6 patients (13.5%). Grade 3 or 4 neuropathy occurred in 4

patients (9.1%). CONCLUSIONS: In gemcitabine-refractory pancreatic cancer, FOLFOX4 showed encouraging activity and was generally well-tolerated. However, careful attention needs to be paid to hematologic toxicities.

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[133]

TÍTULO / TITLE: - Cytoplasmic Clusterin Expression Correlates With Pancreatic Neuroendocrine Tumor Size and Pathological Stage.

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

REVISTA / JOURNAL: - Pancreas. 2013 Aug;42(6):967-970.

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

1097/MPA.0b013e318293734b

AUTORES / AUTHORS: - Henderson-Jackson EB; Nasir A; Chen DT; Nandyala P; Djeu J; Strosberg J; Kvols L; Coppola D

INSTITUCIÓN / INSTITUTION: - From the *Department of Anatomic Pathology, Moffitt Cancer Center and University of South Florida, College of Medicine, Tampa, FL; daggerEli Lilly & Company, Indianapolis, IN; and double daggerBiostatistics Department, Moffitt Cancer Center, Tampa; section signDepartment of Pathology, Oak Hill Hospital, Hudson; and parallelDepartment of Immunology, and paragraph signGatrointestinal Oncology Program, and #Department of Anatomic Pathology and Oncological Sciences, Moffitt Cancer Center and University of South Florida College of Medicine, Tampa, FL.

RESUMEN / SUMMARY: - OBJECTIVES: Cytoplasmic clusterin (Clusterin), a ubiquitous multifunctional secretory sulfated glycoprotein, plays a role in apoptosis and is reportedly overexpressed in a variety of tumors. The role of Clusterin in pancreatic neuroendocrine tumors (PNETs) has not been investigated. In this study, Clusterin expression was evaluated in a subset of PNETs, and the results were correlated with the clinical-pathological features of the tumors. METHODS: Fifty-nine surgical cases were used to evaluate the immunohistochemical expression of Clusterin in PNETs. Using the avidin-biotin complex method, tissue sections from each case were stained with a rabbit anticlusterin antibody (Abcam, Cambridge, Mass). The immunohistochemical reactions were qualitatively and semiquantitatively evaluated by 2 pathologists. RESULTS: Strong Clusterin reactivity was identified in 36 (61%) of 59 PNETs. In 23 (39%) of 59 cases, the Clusterin score was 3 or less. Clusterin expression scores significantly associated with tumor size (P = 0.03) and with tumor stage (P = 0.02). The immunohistochemical score index did not correlate with tumor grade (P = 0.15). CONCLUSIONS: We report the expression of Clusterin in PNETs. The correlation of Clusterin with tumor size and stage suggests involvement of this molecule in pancreatic neuroendocrine tumor progression. Clusterin may represent a new target of therapy for PNETs.

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[134]
TÍTULO / TITLE: - Sweating the small stuff: microRNAs and genetic changes define pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreas. 2013 Jul;42(5):740-59. doi: 10.1097/MPA.0b013e3182854ab0.
●● Enlace al texto completo (gratuito o de pago) 1097/MPA.0b013e3182854ab0
AUTORES / AUTHORS: - Tang S; Bonaroti J; Unlu S; Liang X; Tang D; Zeh HJ; Lotze MT
INSTITUCIÓN / INSTITUTION: - Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA, USA.
RESUMEN / SUMMARY: - MicroRNAs (miRNAs) are 18- to 22-nucleotide-long, single-stranded, noncoding RNAs that regulate important biological processes including differentiation, proliferation, and response to cellular stressors such as hypoxia, nutrient depletion, and traversion of the cell cycle by controlling protein expression within the cell. Many investigators have profiled cancer tissue and serum miRNAs to identify potential therapeutic targets, understand the pathways involved in tumorigenesis, and identify diagnostic tumor signatures. In the setting of pancreatic cancer, obtaining pancreatic tissue is invasive and impractical for early diagnosis. Several groups have profiled miRNAs that are present in the blood as a means to diagnose tumor progression and predict prognosis/survival or drug resistance. Several miRNA signatures found in pancreatic tissue and the peripheral blood, as well as the pathways that are associated with pancreatic cancer, are reviewed here in detail. Three miRNA biomarkers (miR-21, miR-155, and miR-200) have been repetitively identified in both pancreatic cancer tissue and patients' blood. Those miRNAs regulate and are regulated by the central genetic and epigenetic changes observed in pancreatic cancer including p53, transforming growth factor beta, p16(INK4A), BRCA1/2, and Kras. These miRNAs are involved in DNA repair, cell cycle, and cell invasion and also play important roles in promoting metastases.

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[135]
TÍTULO / TITLE: - miR-320c regulates gemcitabine-resistance in pancreatic cancer via SMARCC1.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Br J Cancer. 2013 Jul 23;109(2):502-11. doi: 10.1038/bjc.2013.320. Epub 2013 Jun 25.
●● Enlace al texto completo (gratuito o de pago) 1038/bjc.2013.320
AUTORES / AUTHORS: - Iwagami Y; Eguchi H; Nagano H; Akita H; Hama N; Wada H; Kawamoto K; Kobayashi S; Tomokuni A; Tomimaru Y; Mori M; Doki Y

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Graduate School of Medicine, Osaka University, Yamadaoka 2-2 (E2), Suita, Osaka 565-0871, Japan.

RESUMEN / SUMMARY: - Background:Gemcitabine-based chemotherapy is the standard treatment for pancreatic cancer. However, the issue of resistance remains unresolved. The aim of this study was to identify microRNAs (miRNAs) that govern the resistance to gemcitabine in pancreatic cancer.Methods:miRNA microarray analysis using gemcitabine-resistant clones of MiaPaCa2 (MiaPaCa2-RGs), PSN1 (PSN1-RGs), and their parental cells (MiaPaCa2-P, PSN1-P) was conducted. Changes in the anti-cancer effects of gemcitabine were studied after gain/loss-of-function analysis of the candidate miRNA. Further assessment of the putative target gene was performed in vitro and in 66 pancreatic cancer clinical samples.Results:miR-320c expression was significantly higher in MiaPaCa2-RGs and PSN1-RGs than in their parental cells. miR-320c induced resistance to gemcitabine in MiaPaCa2. Further experiments showed that miR-320c-related resistance to gemcitabine was mediated through SMARCC1, a core subunit of the switch/sucrose nonfermentable (SWI/SNF) chromatin remodeling complex. In addition, clinical examination revealed that only SMARCC1-positive patients benefited from gemcitabine therapy with regard to survival after recurrence (P=0.0463).Conclusion:The results indicate that miR-320c regulates the resistance of pancreatic cancer cells to gemcitabine through SMARCC1, suggesting that miR-320c/SMARCC1 could be suitable for prediction of the clinical response and potential therapeutic target in pancreatic cancer patients on gemcitabine-based therapy.

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[136]

TÍTULO / TITLE: - Primary lymph node gastrinoma: a rare cause of abdominal pain in childhood.

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

REVISTA / JOURNAL: - J Pediatr Hematol Oncol. 2013 Jul;35(5):394-8. doi: 10.1097/MPH.0b013e318298de7e.

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

1097/MPH.0b013e318298de7e

AUTORES / AUTHORS: - Citak EC; Taskinlar H; Arpaci RB; Apaydin FD; Gunay EC; Tanriverdi H; Akyurek N

INSTITUCIÓN / INSTITUTION: - Departments of *Pediatric Oncology daggerPediatric Surgery double daggerPathology section signRadiology parallelNuclear Medicine paragraph signPediatrics, Mersin University Faculty of Medicine, Mersin #Department of Pathology, Gazi University Faculty of Medicine, Ankara, Turkey.

RESUMEN / SUMMARY: - Gastrinoma is a hormone-secreting tumor associated with the Zollinger-Ellison syndrome. It is quite rare among children. The

discovery of gastrinomas in unusual locations such as lymph nodes, bones, ovaries, and the liver poses a diagnostic dilemma as to whether the tumor is primary or metastatic. Here, we present a case of a primary gastrinoma within a lymph node.

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[137]

TÍTULO / TITLE: - Lack of association between occupational exposure to diesel exhaust and risk of pancreatic cancer: a systematic evaluation of available data.

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

REVISTA / JOURNAL: - Int Arch Occup Environ Health. 2013 Jul 13.

●● Enlace al texto completo (gratuito o de pago) 1007/s00420-013-0892-7

AUTORES / AUTHORS: - Boffetta P

INSTITUCIÓN / INSTITUTION: - Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY, 10029, USA, paolo.boffetta@mssm.edu.

RESUMEN / SUMMARY: - PURPOSE: To review epidemiologic studies on risk of pancreatic cancer and occupational exposure to diesel exhaust. METHODS: A literature search was conducted, and data were abstracted in a systematic fashion. Comparable results were combined using a random-effects meta-analysis. RESULTS: Twenty-six studies were included in the review, including five studies based on routine statistics, 11 case-control studies [meta-relative risk (RR) of three estimates for diesel exhaust exposure 0.9; 95 % confidence interval (CI) 0.5, 1.6] and ten cohort studies (meta-RR of their results: 1.03; 95 % CI 0.93, 1.13). Few studies reported results according to duration of exposure or other quantitative measures; no consistent pattern emerged. CONCLUSIONS: The overall evidence from studies on occupational exposure to diesel exhaust and risk of pancreatic cancer leads to the conclusion of the absence of such association.

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[138]

TÍTULO / TITLE: - Aspirin: A Potential Therapeutic Approach in Pancreatic Cancer.

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

REVISTA / JOURNAL: - Curr Med Chem. 2013 Jul 24.

AUTORES / AUTHORS: - Shen X; Han L; Ma Z; Chen C; Duan W; Yu S; Li P; Zhang L; Li W; Xu Q; Ma Q

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. gyma56@mail.xjtu.edu.cn.

RESUMEN / SUMMARY: - Inflammation has become a research hotspot in solid tumours and has been confirmed as a key factor in tumour development through the interactions of inflammatory mediators with gene expression, cell

proliferation, and apoptosis. Pancreatic cancer (PC) is one of the most aggressive and deadliest forms of gastrointestinal cancer. A large case-control study found that aspirin, an anti-inflammatory drug, was associated with a decreased risk of PC. Moreover, aspirin has been shown to have inhibitory effects on PC in both in vitro and in vivo studies. However, the clinical data analysis has not been similarly promising. Results from genetic and pharmacological studies suggest that the anti-tumour effects of aspirin are mediated, at least in part, through the inhibition of COXs. However, other results suggest that the chemopreventive and therapeutic effects of aspirin are also mediated through COX-independent mechanisms. The COX-dependent and COX-independent mechanisms will be described in this review. In addition, we will discuss future research directions on the risks and benefits of the use of aspirin to treat PC and the potential cellular/molecular mechanisms and cellular targets that are involved in its activity.

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[139]

TÍTULO / TITLE: - Non-hyperfunctioning neuroendocrine tumours of the pancreas: MR imaging appearance and correlation with their biological behaviour.

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

REVISTA / JOURNAL: - Eur Radiol. 2013 Jun 21.

●● Enlace al texto completo (gratuito o de pago) 1007/s00330-013-2929-4

AUTORES / AUTHORS: - Manfredi R; Bonatti M; Mantovani W; Graziani R; Segala D; Capelli P; Butturini G; Mucelli RP

INSTITUCIÓN / INSTITUTION: - Department of Radiology, University of Verona, 11 P.le L.A. Scuro 10, 37134, Verona, Italy, riccardo.manfredi@univr.it.

RESUMEN / SUMMARY: - OBJECTIVE: To describe MR imaging features of non-hyperfunctioning neuroendocrine pancreatic tumours by comparing them to histopathology and to determine the accuracy of MR imaging in predicting biological behaviour. MATERIALS AND METHODS: After institutional review board approval, we retrospectively reviewed 45 patients with pathologically proven NF-NET of the pancreas and >/=1 preoperative MR/MRCP examinations. Of the NF-NETS, 29/45 (64.4 %) were G1 and 16/45 (35.5 %) were G2. Image analysis included the lesion maximum diameter, vascular encasement, extrapancreatic spread, signal intensity on T1- and T2-weighted, contrast enhancement features, and presence of metastases. Tumour vessel density was calculated on the histological specimen using a grid. RESULTS: The median maximum diameter of NF-NETs was 20 mm (range 5-200 mm). Eighty per cent of the NF-NETs were hypointense on T1-weighted images, 82.2 % were hyperintense on T2-weighted images, and 75.6 % were hypervascular. Overall MRI accuracy showed a mean AUC of 0.86 compared to pathology. Lesions with a maximum diameter of 30 mm irregular margins, absence of a

cleavage plane with the main pancreatic duct, vascular encasement, extrapancreatic spread and abdominal metastases were significantly associated with malignant NF-NETs. No correlation was found between the tumour vessel density and contrast-enhanced MR imaging pattern. CONCLUSIONS: Hyperintensity on T2-weighted images and iso-/hypervascularity occurred in 27/45 (60.0 %) of NF-NETs. MRI identifies malignant NF-NETs with a sensitivity of 93.3 % and a specificity of 76.9 % (AUC = 0.85). KEY POINTS: * Non-hyperfunctioning neuroendocrine pancreatic tumours (NF-NET) pose a difficult diagnostic challenge. * On T2-weighted MRI, 82.2 % of neuroendocrine tumours appeared hyperintense. * MR imaging showed 0.94 sensitivity and 0.77 specificity in predicting biological behaviour. * The hyper-/isointensity during dynamic MRI did not correlate with vessel density at pathology.

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[140]

TÍTULO / TITLE: - Is intraductal papillary mucinous neoplasm associated with extrapancreatic malignancies? Which is the true, prevalence or incidence?

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

REVISTA / JOURNAL: - Ann Oncol. 2013 Aug;24(8):2196. doi: 10.1093/annonc/mdt256.

●● Enlace al texto completo (gratuito o de pago) 1093/annonc/mdt256

AUTORES / AUTHORS: - Kawakubo K; Tada M; Koike K

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo.

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[141]

TÍTULO / TITLE: - Imaging features of pancreatic tumors in children: 13-year experience at a pediatric tertiary hospital.

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

REVISTA / JOURNAL: - Pediatr Radiol. 2013 Jun 7.

●● Enlace al texto completo (gratuito o de pago) 1007/s00247-013-2721-2

AUTORES / AUTHORS: - Ahmed TS; Chavhan GB; Navarro OM; Traubici J

INSTITUCIÓN / INSTITUTION: - Department of Medical Imaging, University of Toronto, 555 University Ave., Toronto, ON, M5G 1X8, Canada.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic tumors are rare in children, resulting in limited information regarding their frequency and imaging appearances. OBJECTIVE: To review all pancreatic tumors seen in children over a decade at a large tertiary pediatric institution and to describe multimodality imaging findings. MATERIALS AND METHODS: We conducted a retrospective review of imaging studies performed in children with pancreatic tumors between January 2000 and December 2012, analyzing imaging features on available US, CT and MR examinations. We reviewed patient charts for

clinical features, management and final diagnosis. RESULTS: We included 23 children in this study. Of these, 12 had solid and papillary epithelial neoplasms (SPEN), 3 had neuroendocrine tumors, 3 had lymphoma, and 1 each had hemangioendothelioma, benign congenital cysts with adipose tissue, dendritic cell sarcoma, metastatic rhabdomyosarcoma, and lipoma. All children with SPEN were teenage girls. SPEN showed characteristic imaging features including well-defined margins with surrounding capsule, solid-cystic components and hemorrhage. CONCLUSION: Pancreatic tumors are uncommon in children. SPEN is the most common tumor and is seen predominantly in teenage girls and shows characteristic imaging features.

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[142]

TÍTULO / TITLE: - Staging accuracy of MR for pancreatic neuroendocrine tumor and imaging findings according to the tumor grade.

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

REVISTA / JOURNAL: - Abdom Imaging. 2013 Jun 2.

●● Enlace al texto completo (gratuito o de pago) 1007/s00261-013-0011-y

AUTORES / AUTHORS: - Kim JH; Eun HW; Kim YJ; Han JK; Choi BI

INSTITUCIÓN / INSTITUTION: - Department of Radiology and Institute of Radiation Medicine, Seoul National University College of Medicine, 101 Daehang-no, Chongno-gu, Seoul, 110-744, Republic of Korea, Jhkim2008@gmail.com.

RESUMEN / SUMMARY: - PURPOSE: To investigate staging accuracy of MR for pancreatic neuroendocrine neoplasms (PNETs) and imaging findings according to the tumor grade. MATERIALS AND METHODS: Our study consisted of 39 patients with PNET G1 (n = 24), PNET G2 (n = 12), and pancreatic neuroendocrine carcinoma (PNEC) (n = 3). All underwent preoperative MRI. Two radiologists retrospectively reviewed MR findings including tumor margin, SI on T2WI, enhancement patterns, degenerative change, duct dilation, and ADC value. They also assessed T-stage, N-stage, and tumor size. Statistical analyses were performed using Chi square tests, ROC analysis, and Fisher's exact test. RESULTS: Specific findings for PNEC or PNET G2 were ill-defined borders (P = 0.001) and hypo-SI on venous- and delayed-phase (P = 0.016). ADC value showed significant difference between PNET G1 and G2 (P = 0.007). The Az of ADC value for differentiating PNET G1 from G2 was 0.743. Sensitivity and specificity were 70% and 86%. Accuracy for T-staging was 77% (n = 30) and 85% (n = 33), and for N-staging was 92% (n = 36) and 87% (n = 34) with moderate agreement. T-stage showed significant difference according to tumor grade (P < 0.001), although there was no significant difference in tumor size or N-stage. CONCLUSION: Ill-defined borders and hypo-SI on venous- and delayed-phase imaging are common findings of higher grade PNET, and ADC value is helpful for differentiating PNET G1 from G2. MR is

useful for preoperative evaluation of T-, N-stage. Tumor size of PNET and T-stage showed significant difference according to tumor grade.

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[143]

TÍTULO / TITLE: - MicroRNA from Pancreatic Duct Aspirate Differentiates Cystic Lesions of the Pancreas.

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

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Jul 25.

●● Enlace al texto completo (gratuito o de pago) 1245/s10434-013-3138-8

AUTORES / AUTHORS: - Henry JC; Bassi C; Giovinazzo F; Bloomston M

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The Ohio State University Wexner Medical Center, Columbus, OH, USA.

RESUMEN / SUMMARY: - INTRODUCTION: Prognostication for cystic neoplasms of the pancreas continues to evolve. Beyond simple size and cystic fluid CEA determination, microRNA (miRNA) detection holds great promise as molecular diagnostics for cancer risk. In this study, we sought to identify miRNAs that could predict malignant potential of pancreatic cystic lesions. METHODS: RNA was harvested from the pancreatic duct aspirate of 72 cystic neoplasms of the pancreas. Samples with adequate RNA concentration (>/=3 ng/muL) were selected for qRTPCR profiling using assays to 379 of the most common miRNAs. miRNA profiles were correlated with histopathology from resected specimens and grouped by benign (serous cystadenomas), premalignant (intraductal papillary mucinous neoplasms and mucinous cystadenomas), or malignant lesions (adenocarcinoma). RESULTS: Adequate RNA for analysis was obtained from 42 (58.3 %) of the samples. Malignant lesions were more likely to have adequate RNA (n = 17, 81 %) than either benign (n = 6, 33 %) or premalignant lesions (n = 19, 59 %; p = 0.011). Nine miRNA were identified as differentially expressed between benign and premalignant/malignant lesions (p < 0.05). A significant correlation was found between the number of differentially expressed miRNA and the likelihood of a premalignant/malignant lesion. All premalignant or malignant lesions expressed at least one miRNA surpassing the threshold of mean miRNA expression, whereas no benign lesions had more than one miRNA surpassing the threshold. CONCLUSIONS: The presence of RNA in the duct aspirate from patients with pancreatic cystic neoplasms may be a predictor of premalignancy or malignancy. miRNA may be utilized to further differentiate between benign, premalignant, and malignant cystic lesions of the pancreas.

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[144]

TÍTULO / TITLE: - Upregulation of extrinsic apoptotic pathway in curcumin-mediated antiproliferative effect on human pancreatic carcinogenesis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Cell Biochem. 2013 Jun 21. doi: 10.1002/jcb.24612.
●● Enlace al texto completo (gratuito o de pago) 1002/jcb.24612
AUTORES / AUTHORS: - Youns M; Fathy G
INSTITUCIÓN / INSTITUTION: - Department of Functional Genome Analysis, German Cancer Research Center (DKFZ), Im Neuenheimer Feld 580, 69120, Heidelberg, Germany; Department of Biochemistry and Molecular Pharmacology, Faculty of Pharmacy, Helwan University, Cairo, Egypt.
RESUMEN / SUMMARY: - Pancreatic cancer is one of the most lethal human cancers, with almost identical incidence and mortality rates. Curcumin, derived from the rhizome of Curcuma longa, has a long history of use as coloring agent and for a wide variety of disorders. Here, the antiproliferative activity of curcumin and its modulatory effect on gene expression of pancreatic cancer cell lines were investigated. The effect of curcumin on cellular proliferation and viability was monitored by sulphurhodamine B assay. Apoptotic effect was evaluated by flow cytometry and further confirmed by measuring amount of cytoplasmic histone-associated DNA fragments. Analysis of gene expression was performed with and without curcumin treatment using microarray expression profiling techniques. Array results were confirmed by real-time PCR. Ingenuity Pathway Analysis (IPA) has been used to classify the list of differentially expressed genes and to indentify common biomarkergenes modulating the chemopreventive effect of curcumin. Results showed that curcumin induces growth arrest and apoptosis in pancreatic cancer cell lines. Its effect was more obvious on the highly COX-2 expressing cell line. Additionally, the expression of 366 and 356 cancer-related genes, involved in regulation of apoptosis, cell cycle, metestasis, was significantly altered after curcumin treatment in BxPC-3 and MiaPaCa-2 cells, respectively. Our results suggested that up-regulation of the extrinsic apoptotic pathway was among signaling pathways modulating the growth inhibitory effects of curcumin on pancreatic cancer cells. Curcumin effect was mediated through activation of TNFR, CASP 8, CASP3, BID, BAX and down-regulation of NFkappaB, NDRG 1 and BCL2L10 genes. J. Cell. Biochem. © 2013 Wiley Periodicals, Inc.

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[145]
TÍTULO / TITLE: - Comparison of various online strategies to account for interfractional variations for pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Aug 1;86(5):914-21. doi: 10.1016/j.ijrobp.2013.04.032.
●● Enlace al texto completo (gratuito o de pago) 1016/j.ijrobp.2013.04.032
AUTORES / AUTHORS: - Ahunbay EE; Kimura B; Liu F; Erickson BA; Li XA

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, Wisconsin. Electronic address: eahunbay@mcw.edu.

RESUMEN / SUMMARY: - PURPOSE: To identify practical techniques to address the large interfractional variations for pancreas irradiation by comparing various used/proposed online strategies. METHODS AND MATERIALS: The daily computed tomography (CT) images acquired using a respiration-gated in-room CT (CTVision; Siemens) for 10 pancreatic cancer patients treated with image guided radiation therapy (IGRT) were analyzed. The contours of the pancreas and organs at risk on each daily CT set were generated by populating from the planning CT using a deformable registration tool (ABAS; Elekta) with manual editing. Nine online strategies were considered: (1) standard IGRT (ie, IGRT with 0-mm additional margin [AM]); (2) IGRT with 2-mm AM; (3) IGRT with 5-mm AM; (4) IGRT with plan renormalized to maintain 95% planning target volume (PTV) coverage; (5) full-scale reoptimization; (6) reoptimization starting from the original plan; (7) segment aperture morphing (SAM) from the original plan, based on PTV shape change; (8) SAM plus segment weight optimization; and (9) reoptimization starting from the SAM plan. One-way analysis of variance was applied to plan qualities for the 9 strategies to assess statistical significance in difference. RESULTS: The 3 IGRT strategies (1-3) lead to either inadequate PTV coverage or higher doses to critical structures, indicating that the additional margins alone are not adequate to account for the changes. The full-scale reoptimization results in the best plan but requires the delineation of several structures, which is time consuming. The SAM strategy (7) was the fastest one, because it requires delineating only 1 structure (target), and its plan quality was comparable to that for the full-scale reoptimization. CONCLUSION: Online replanning strategies can lead to either reduced organs-at-risk dose and/or improved target coverage as compared with the current practice of IGRT. The SAM-based online replanning is comparable to full-scale reoptimization and is efficient for practical use.

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[146]

TÍTULO / TITLE: - Intestinal and pancreatobiliary differentiation in periampullary carcinoma: the role of immunohistochemistry.

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

REVISTA / JOURNAL: - Hum Pathol. 2013 Jul 5. pii: S0046-8177(13)00188-3. doi: 10.1016/j.humpath.2013.05.003.

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

1016/j.humpath.2013.05.003

AUTORES / AUTHORS: - Kumari N; Prabha K; Singh RK; Baitha DK; Krishnani N

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 266014, India. Electronic address: niraj@sgpgi.ac.in.

RESUMEN / SUMMARY: - Periampullary carcinoma (PC) is classified into intestinal and pancreatobiliary subtypes using morphology and immunohistochemistry (IHC). Different combinations of markers have been used in the literature. One hundred eight PCs were classified using morphology and IHC (CDX2, mucin [MUC] 2, cytokeratin [CK] 20, CK7, CK17, and MUC1). The expression of these markers was compared with different histologic subtypes, histopathologic prognostic parameters, and patients' survival. There were 38 intestinal and 53 pancreatobiliary subtypes classified on morphology alone. CDX2 showed high sensitivity (89.5%) and specificity (100%) for intestinal type. CK20 and MUC2 showed low sensitivity (50% and 39.5%) but high specificity (86.8% and 96.2%) for intestinal type. CK7 and CK17 showed a sensitivity of 90.5% and 32% and a specificity of 21% and 89.4%, respectively, for pancreatobiliary subtype. MUC1 was 100% sensitive but 0% specific in pancreatobiliary subtype. The overall median survival in morphologic and IHC intestinal type was 45 months versus 20 months in pancreatobiliary type (P = 0.01). Intestinal and pancreatobiliary types of PC were differentiated in 84.2% of cases by morphology alone and in 87.9% cases with IHC. CDX2-positive tumors had a median survival of 44 months versus 22 months in CDX2-negative tumors (P = .03). IHC helped in reclassifying an additional 4 cases of mixed and other types. Among the panel used, CDX2 showed a high sensitivity and specificity for intestinal subtype and was an independent prognostic marker for longer survival. Thus, CDX2 may be used routinely with morphology in subtyping of PC, and a panel of markers may be used in morphologically difficult cases.

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[147]

TÍTULO / TITLE: - Circulating microparticle tissue factor, thromboembolism and survival in pancreaticobiliary cancers.

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

REVISTA / JOURNAL: - Thromb Res. 2013 Jul 12. pii: S0049-3848(13)00277-6. doi: 10.1016/j.thromres.2013.06.026.

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

1016/j.thromres.2013.06.026

AUTORES / AUTHORS: - Bharthuar A; Khorana AA; Hutson A; Wang JG; Key NS; Mackman N; Iyer RV

INSTITUCIÓN / INSTITUTION: - Departments of Medicine and Biostatistics, Roswell Park Cancer Institute, Buffalo, N.Y. USA.

RESUMEN / SUMMARY: - BACKGROUND: Tissue factor (TF), the physiologic initiator of coagulation, is over-expressed in pancreatic cancer, and is associated with a pro-coagulant and pro-angiogenic state. We hypothesized that in patients with pancreaticobiliary cancers (PBC), elevated circulating microparticle-associated TF (MP-TF) activity would be associated with thrombosis and worsened survival. PATIENTS AND METHODS: Clinical data

and plasma were obtained for consecutive patients with PBC seen at Roswell Park Cancer Institute from 2005-08. MP-TF activity levels were measured using a TF-dependent FXa generation assay. RESULTS: The study population comprised 117 patients, including pancreatic (n=80), biliary (n=34) or unknown primary histologically consistent with PBC (n=3). Of these, 52 patients (44.5%) experienced thromboembolism, including pulmonary embolism (n=15), deep venous thrombosis (n=21) and other arterial or venous events (n=32). Mean TF was 2.15 (range 0.17- 31.01) pg/mL. Median survival was 98.5days for MP-TF activity >/=2.5pg/mL versus 231days for MP-TF activity<2.5pg/mL (p<0.0001). In multivariate analysis, elevated MP-TF activity was associated with both VTE (OR 1.4, 95% CI 1.1-1.6) and mortality (HR 2.5, 95% CI 1.4-4.5). CONCLUSIONS: Elevated circulating MP-TF activity is associated with thrombosis and worsened survival in patients with PBC. MP-TF activity as a prognostic biomarker warrants further prospective evaluation.

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[148]

TÍTULO / TITLE: - Evidence that P12, a specific variant of P16(INK4A), plays a suppressive role in human pancreatic carcinogenesis.

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

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Jun 28;436(2):217-22. doi: 10.1016/j.bbrc.2013.05.078. Epub 2013 May 29.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bbrc.2013.05.078

AUTORES / AUTHORS: - Poi MJ; Knobloch TJ; Yuan C; Tsai MD; Weghorst CM; Li J

INSTITUCIÓN / INSTITUTION: - Department of Pharmacy, The Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, The Ohio State University, Columbus, OH 43210, United States.

RESUMEN / SUMMARY: - The INK4a-ARF locus plays a central role in the development of pancreatic tumors as evidenced by the fact that up to 98% of pancreatic tumor specimens harbored genetic alterations at the INK4a-ARF locus. Interestingly, in addition to the well-known P16(INK4A) (P16) and P14ARF tumor suppressors, the INK4a-ARF locus in pancreas encodes another protein, P12, whose structure, function, and contributions to pancreatic carcinogenesis remain to be elucidated. In the current study, we demonstrated that over-expression of p12 in human pancreatic cancer cells led to cell arrest at the G1 phase and such cell cycle arrest was related to down-regulation of a number of oncogenes, such as c-Jun, Fos, and SEI1. Furthermore, unlike P16, P12 did not retain any cyclin-dependent kinase 4 (CDK4)-inhibitory activity. Instead, P12 exhibited a transactivating activity not found in P16. We also examined the genetic status of p12 in a cohort of 40 pancreatic tumor specimens and found that p12 alteration was prevalent in pancreatic tumors with an incidence of 70% (28/40). These results support that P12 is a tumor

suppressive protein distinct from P16, and its genetic inactivation is associated with pancreatic carcinogenesis.

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[149]

TÍTULO / TITLE: - Autologous Islet Transplantation After Total Pancreatectomy for Renal Cell Carcinoma Metastases.

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

REVISTA / JOURNAL: - Am J Transplant. 2013 Jul 16. doi: 10.1111/ajt.12354.

●● Enlace al texto completo (gratuito o de pago) 1111/ajt.12354

AUTORES / AUTHORS: - Gala-Lopez BL; Semlacher E; Manouchehri N; Kin T; Shapiro AM

INSTITUCIÓN / INSTITUTION: - Clinical Islet Transplant Program, University of Alberta, Alberta, Canada; Department of Surgery, University of Alberta, Alberta, Canada.

RESUMEN / SUMMARY: - Pancreatic metastases from renal cell carcinoma (RCC) may have a chronic and highly indolent course, and may be resected for cure after considerable delay following treatment of the primary tumor, in contrast to other more common pancreatic tumors. Surgical resection is the treatment of choice, which may lead to postpancreatectomy diabetes mellitus in the case of extensive resection. We present a 70-year-old patient with multifocal pancreatic metastases from RCC causing obstructive jaundice. A total pancreatectomy was required to excise two distant tumors in the head and tail of the pancreas, together with a segment VI liver resection. An autologous islet transplant (AIT) prepared from the central, uninvolved pancreas was carried out to prevent postpancreatectomy diabetes. The patient was rendered insulin-free and remains so with excellent glycemic control for 1 year of follow-up, and there is no evidence of tumor recurrence. The patient has been treated with adjuvant sunitinib to minimize risk of further recurrence. In conclusion, AIT after pancreatectomy may represent a useful option to treat patients with metastatic RCC. A critical component of this approach was dependent upon elaborate additional testing to exclude contamination of the islet preparation by cancerous cells.

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[150]

TÍTULO / TITLE: - An extended fluorescence in situ hybridization approach for the cytogenetic study of cholangiocarcinoma on endoscopic retrograde cholangiopancreatography brushing cytology preparations.

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

REVISTA / JOURNAL: - Hum Pathol. 2013 Jul 8. pii: S0046-8177(13)00181-0. doi: 10.1016/j.humpath.2013.04.012.

●● Enlace al texto completo (gratuito o de pago) 1016/j.humpath.2013.04.012

AUTORES / AUTHORS: - Vasilieva LE; Papadhimitriou SI; Alexopoulou A; Pavlidis D; Kostopoulos I; Georgiakaki M; Xinopoulos D; Romanos A; Dourakis SP

INSTITUCIÓN / INSTITUTION: - 2nd Department of Internal Medicine, University of Athens Medical School, Athens, Greece. Electronic address: larisatheo@yahoo.gr.

RESUMEN / SUMMARY: - The cytological diagnosis of cholangiocarcinoma has been significantly aided by applying a 4-probe fluorescence in situ hybridization system on endoscopic retrograde cholangiopancreatography brushing smears, aiming mainly at the detection of hyperdiploidy. However, this approach adds little to our understanding of the genetic background of the disease. With the prospect of obtaining additional data on chromosomal aberrations, we have extended the fluorescence in situ hybridization study, with the application of 4 independent 2-probe systems in 35 patients with documented cholangiocarcinoma. Fluorescence in situ hybridization assays were performed on endoscopic retrograde cholangiopancreatography brushing smears, with probes for the 7q31, 11q13 (CCND1), 17p53 (TP53), and 9p21 (INK4 locus) bands, together with the respective centromeric probe. Hyperdiploidy, involving at least 2 of the 4 chromosomes targeted, was found in 31 patients. 17p13 deletion was detected in 3, and 9p21 deletion, in 5 of the hyperdiploid cases, with the 2 aberrations concurrent in 1. CCND1 amplification was found in 1 case as the sole abnormality and in another together with hyperdiploidy, but in apparently unrelated clones. This work indicates that interphase fluorescence in situ hybridization is a practical and useful tool for the cytogenetic study of cholangiocarcinoma on endoscopic retrograde cholangiopancreatography brushing smears, which is often the only available tissue specimen of the tumor. Apart from hyperdiploidy, it provides additional data on the genetic profile of cholangiocarcinoma, especially regarding structural chromosomal aberrations and clonal diversity. This line of investigation may prove useful in the delineation of oncogenesis and the interpretation of the diverse clinical features of the disease.

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[151]

TÍTULO / TITLE: - The CX3CL1/CX3CR1 reprogrammes glucose metabolism through HIF-1 pathway in pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - J Cell Biochem. 2013 Jul 16. doi: 10.1002/jcb.24608.

●● Enlace al texto completo (gratuito o de pago) 1002/jcb.24608

AUTORES / AUTHORS: - Ren H; Zhao T; Sun J; Wang X; Liu J; Gao S; Yu M; Hao J

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

RESUMEN / SUMMARY: - One of the hallmarks of cancer is revised glucose metabolism that promotes cell survival and 'proliferation. In pancreatic cancer, the regulatory mechanism of glucose metabolism remains to be elucidated. In this study, we found that CX3CR1 is expressed in pancreatic cancer cells lines. exogenous or transfected CX3CL1 increased glucose uptake and lactate secretion. CX3CL1 stimulated HIF-1 expression through PI3K/Akt and MAPK pathways. Furthermore, knockdown of HIF-1 blocked CX3CL1-modified glucose metabolism in pancreatic adenocarcinoma cells. In conclusion, the CX3CL1/CX3CR1 reprogrammes glucose metabolism through HIF-1 pathway in pancreatic cancer cells. J. Cell. Biochem. © 2013 Wiley Periodicals, Inc.

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[152]

TÍTULO / TITLE: - Three-Dimensional Contrast-Enhanced Ultrasonography of Intraductal Papillary Mucinous Neoplasms of the Pancreas: A Comparison With Magnetic Resonance Imaging.

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

REVISTA / JOURNAL: - Pancreas. 2013 Jun 13.

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

1097/MPA.0b013e318291fbe5

AUTORES / AUTHORS: - Pezzilli R; Serra C; Calculli L; Ferroni F; Iammarino MT; Casadei R

INSTITUCIÓN / INSTITUTION: - From the Departments of *Digestive Diseases and Internal Medicine, daggerRadiology, and double daggerSurgery, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy.

RESUMEN / SUMMARY: - OBJECTIVES: The objective of this study was to prospectively compare the diagnostic accuracy of 3-dimensional contrast-enhanced ultrasonography (3D-CEUS) with that of magnetic resonance imaging (MRI) in the study of intraductal papillary mucinous neoplasms (IPMNs) of the pancreas. METHODS: Thirty consecutive patients with IPMN were studied. RESULTS: Three patients (10.0%) did not undergo diagnostic 3D-CEUS because of technical problems. Three dimensional CEUS identified 12 (44.4%) main-duct IPMNs versus no cases by MRI (P < 0.001). Intraductal papillary mucinous neoplasm localization showed poor agreement between 3D-CEUS and MRI (kappa = 0.058), whereas good agreement was found in detecting the pancreatic calcifications (kappa = 1.000). Significant differences between 3D-CEUS and MRI were found regarding the number of lesions detected (1.4 +/- 0.8 vs 3.8 +/- 3.6; P < 0.001), the detection of mucinous plugs (3.7% vs 50.0%; P < 0.001), chronic pancreatitis (7.4% vs 26.7%; P = 0.031), pancreatic atrophy (0% vs 50.0%; P < 0.001), thick septa (22.2% vs 53.3%; P = 0.004), and mural nodules (25.9% vs 3.3%; P = 0.016). Three dimensional CEUS showed similar results as compared with MRI in evaluating IPMNs smaller than 1 cm of diameter or greater than 2 cm. CONCLUSIONS: Even if

MRI remains the criterion standard technique for the diagnosis of IPMNs, 3D-CEUS can be safely used to follow patients with IPMNs of less than 1 cm.

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[153]

TÍTULO / TITLE: - Endoscopically Acquired Pancreatic Cyst Fluid MicroRNA 21 and 221 Are Associated With Invasive Cancer.

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

REVISTA / JOURNAL: - Am J Gastroenterol. 2013 Aug;108(8):1352-9. doi: 10.1038/ajg.2013.167. Epub 2013 Jun 11.

●● Enlace al texto completo (gratuito o de pago) 1038/ajg.2013.167

AUTORES / AUTHORS: - Farrell JJ; Toste P; Wu N; Li L; Wong J; Malkhassian D; Tran LM; Wu X; Li X; Dawson D; Wu H; Donahue TR

INSTITUCIÓN / INSTITUTION: - Section of Digestive Diseases, Yale Center for Pancreatic Disease, Yale SOM, New Haven, Connecticut, USA.

RESUMEN / SUMMARY: - OBJECTIVES: Pancreatic cysts are a group of lesions with heterogeneous malignant potential. Currently, there are no reliable biomarkers to aid in cyst diagnosis and classification. The objective of this study was to identify potential microRNA (miR) biomarkers in endoscopically acquired pancreatic cyst fluid that could be used to distinguish between benign, premalignant, and malignant cysts. METHODS: A list of candidate miRs was developed using a whole-genome expression array analysis of pancreatic cancer (pancreatic ductal adenocarcinoma) and nonmalignant samples overlapped with existing literature and predicted gene targets. Endoscopically acquired pancreatic cyst fluid samples were obtained from a group of 38 patients who underwent cyst fluid aspiration and surgical resection. Selected miR expression levels in cyst fluid samples were assessed by quantitative real-time-PCR. Additionally, in situ hybridization (ISH) on corresponding cyst tissue samples was performed to identify the source and validate the expression level of fluid miRs. RESULTS: Of the six miRs that were profiled in the study, two showed differential expression in malignant cysts. miR-221 was expressed at significantly higher levels in malignant cysts compared with benign or premalignant cysts (P=0.05). miR-21 was also expressed at significantly higher levels in malignant cysts (P<0.01). Additionally, the expression of miR-21 was significantly higher in premalignant cysts than benign cysts (P=0.03). The differential expression of miR-21 among cyst categories was confirmed by ISH. CONCLUSIONS: In this small single-center study, miRs are potential pancreatic cyst fluid diagnostic biomarkers. In particular, miR-21 is identified as a candidate biomarker to distinguish between benign, premalignant, and malignant cysts. Additionally miR-221 may be of use in the identification of more advanced malignant disease.

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[154]

TÍTULO / TITLE: - eEF1A2 promotes cell migration, invasion and metastasis in pancreatic cancer by upregulating MMP-9 expression through Akt activation.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Exp Metastasis. 2013 Jun 6.
●● Enlace al texto completo (gratuito o de pago) 1007/s10585-013-9593-6
AUTORES / AUTHORS: - Xu C; Hu DM; Zhu Q
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Rui Jin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, 200025, China.
RESUMEN / SUMMARY: - eEF1A2 is a protein translation factor involved in protein synthesis that is overexpressed in various cancers, with important functions in tumor genesis and progression. We have previously showed that the ectopic expression of eEF1A2 is correlated with lymph node metastasis and perineural invasion in pancreatic cancer. In this study, we investigated the functional role of eEF1A2 in the regulation of cell migration, invasion, and metastasis in pancreatic cancer. Furthermore, we investigated the potential molecular mechanisms involved. By evaluating the invasive ability of a panel of pancreatic cancer cell lines with different metastatic potentials, eEF1A2 expression in cells was positively associated with their invasive ability. The knockdown of eEF1A2 by siRNA decreased the migration and invasion of PANC-1 cells. By contrast, the ectopic expression of exogenous eEF1A2 significantly promoted the migration and invasion of SW1990 cells. Stable eEF1A2 overexpression in a nude mouse model of peritoneal metastasis likewise dramatically enhanced the intraperitoneal metastatic ability of SW1990 cells. In addition, eEF1A2 overexpression could upregulate MMP-9 expression and activity. A significant positive correlation between the overexpression of both eEF1A2 and MMP-9 was observed in pancreatic cancer tissues. The inhibition of MMP-9 activity reduced the promoting effect of eEF1A2 on cell migration and invasion. Furthermore, eEF1A2-mediated cell migration and invasion, as well as MMP-9 expression and upregulation, were largely dependent on the eEF1A2-induced Akt activation. The findings suggested the potentially important role of eEF1A2 in pancreatic cancer migration, invasion, and metastasis. Thus, the results provide evidence of eEF1A2 as a potential therapeutic target in the treatment of aggressive pancreatic cancer.

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[155]
TÍTULO / TITLE: - BAG3 Is a Novel Serum Biomarker for Pancreatic Adenocarcinomas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Am J Gastroenterol. 2013 Jul;108(7):1178-80. doi: 10.1038/ajg.2013.128.
●● Enlace al texto completo (gratuito o de pago) 1038/ajg.2013.128

AUTORES / AUTHORS: - Falco A; Rosati A; Festa M; Basile A; De Marco M; d'Avenia M; Pascale M; Dal Piaz F; Tavano F; Di Mola FF; di Sebastiano P; Berloco PB; Nudo F; Caraglia M; Febbraro A; Barcaroli D; Scarpa A; Pezzilli R; De Laurenzi V; Turco MC

INSTITUCIÓN / INSTITUTION: - 1] Department of Pharmaceutical and Biomedical Sciences (FARMABIOMED), University of Salerno, Fisciano (SA), Italy [2] BIOUNIVERSA, University of Salerno, Fisciano (SA), Italy [3] These authors contributed equally to this work.

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[156]

TÍTULO / TITLE: - The Expression of S100A4 in Human Pancreatic Cancer Is Associated With Invasion.

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

REVISTA / JOURNAL: - Pancreas. 2013 Aug;42(6):1027-33. doi: 10.1097/MPA.0b013e31828804e7.

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

1097/MPA.0b013e31828804e7

AUTORES / AUTHORS: - Tsukamoto N; Egawa S; Akada M; Abe K; Saiki Y; Kaneko N; Yokoyama S; Shima K; Yamamura A; Motoi F; Abe H; Hayashi H; Ishida K; Moriya T; Tabata T; Kondo E; Kanai N; Gu Z; Sunamura M; Unno M; Horii A

INSTITUCIÓN / INSTITUTION: - From the *Departments of Pathology and; daggerSurgery, Tohoku University School of Medicine; and double daggerDepartment of Pathology, Tohoku University Hospital, Sendai; and section signDepartment of Digestive Tract Surgery and Transplantation Surgery, Tokyo Medical University Hachioji Medical Center, Tokyo, Japan.

RESUMEN / SUMMARY: - OBJECTIVES: Pancreatic cancer is one of the most lethal malignancies; its poor prognosis is strongly associated with invasion and metastasis. Expression of S100A4 has been reported to correlate with poor prognosis in various cancers. We have investigated the role of S100A4 in pancreatic cancer tumorigenesis and its clinicopathologic significance. METHODS: Protein expression of S100A4 was examined by Western blot in pancreatic cancer cell lines and a human pancreatic ductal epithelium cell line, HPDE-6. Then the expressions of S100A4, TP53, and CD133 were examined immunohistochemically in resected specimens from 83 patients with pancreatic cancer to clarify their clinicopathologic significance. Survival analyses were performed using the Kaplan-Meier method and the Mantel-Cox method. RESULTS: Forty-eight (58%) of 83 patients with pancreatic cancer positively expressed S100A4, and 50 (60%) and 29 (36%) patients positively expressed TP53 and CD133, respectively. S100A4 expression was significantly correlated with perineural invasion (P = 0.029) and invasion pattern (P = 0.001). Neither TP53 nor CD133 expression showed significant correlations with any other parameters. CONCLUSIONS: Our present results suggest that S100A4 plays

an important role in the invasiveness, particularly with perineural invasion and invasion pattern, of pancreatic cancer. Development of new strategies targeting S100A4 or its downstream effectors is warranted.

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[157]

TÍTULO / TITLE: - Rare ALK Expression but no ALK Rearrangement in Pancreatic Ductal Adenocarcinoma and Neuroendocrine Tumors.

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

REVISTA / JOURNAL: - Pancreas. 2013 Aug;42(6):949-51. doi: 10.1097/MPA.0b013e3182847bd0.

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

1097/MPA.0b013e3182847bd0

AUTORES / AUTHORS: - Graham RP; Oliveira AM; Zhang L

INSTITUCIÓN / INSTITUTION: - From the Division of Anatomic Pathology, Mayo Clinic, Rochester, MN.

RESUMEN / SUMMARY: - OBJECTIVES: Anaplastic lymphoma kinase (ALK) gene rearrangements were first identified in anaplastic large cell lymphomas. Subsequently, they have been observed in other tumor types with ALK-rearranged tumors demonstrating responsiveness to ALK inhibitors. The aggressiveness of pancreatic ductal adenocarcinoma warrants the examination of ALK rearrangements in pancreatic cancer as a potential therapeutic target. Immunohistochemical expression of ALK1 correlates with ALK rearrangements in other tumors. We performed ALK immunohistochemistry on samples of pancreatic ductal adenocarcinoma and pancreatic neuroendocrine tumors using 2 tissue microarrays. METHODS: ALK1 expression was scored for each case as 0, 1+, 2+, or 3+ using established criteria. Fluorescence in situ hybridization using a break-apart assay with probes for ALK was performed to detect ALK rearrangement in ALK1-positive cases. RESULTS: All 46 neuroendocrine tumors were negative for ALK1. Of 140 ductal adenocarcinoma cases, 5 showed immunoreactivity for ALK1: 1 was 3+, 2 were 2+, and 2 were 1+. However, fluorescence in situ hybridization for ALK rearrangement was negative in all 5 cases. CONCLUSIONS: The results demonstrate that ALK1 expression is uncommon in both pancreatic ductal adenocarcinoma and neuroendocrine tumors. Rare ALK1 expression is not induced by ALK translocation, and ALK is unlikely to be a therapeutic target in pancreatic tumors.

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[158]

TÍTULO / TITLE: - An engineered anti-CA19-9 cys-diabody for positron emission tomography imaging of pancreatic cancer and targeting of polymerized liposomal nanoparticles.

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

REVISTA / JOURNAL: - J Surg Res. 2013 Jun 19. pii: S0022-4804(13)00577-5. doi: 10.1016/j.jss.2013.05.095.

●● Enlace al texto completo (gratuito o de pago) 1016/j.jss.2013.05.095

AUTORES / AUTHORS: - Girgis MD; Federman N; Rochefort MM; McCabe KE; Wu AM; Nagy JO; Denny C; Tomlinson JS

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Veterans Healthcare Affairs, Greater Los Angeles, Los Angeles, California; Department of Surgery, UCLA, Los Angeles, California.

RESUMEN / SUMMARY: - BACKGROUND: Antibody-based therapeutics is a rapidly growing field. Small engineered antibody fragments demonstrate similar antigen affinity compared with the parental antibody but have a shorter serum half-life and possess the ability to be conjugated to nanoparticles. The goal of this study was to engineer an anti-carbohydrate antigen 19-9 (CA19-9) cys-diabody fragment in hopes of targeting nanoparticles to pancreatic cancer. METHODS: The anti-CA19-9 cys-diabody was created by engineering a C-terminal cysteine residue into the DNA single-chain Fv construct of the anti-CA19-9 diabody and expressed in NS0 cells. Maleimide chemistry was used to conjugate the cys-diabody to polymerized liposomal nanoparticles (PLNs) through the cysteine residues. Flow cytometry was used to evaluate targeting of cys-diabody and cys-diabody-PLN conjugate to human pancreatic cancer cell lines. The cys-diabody was radiolabeled with a positron emitter (124I) and evaluated in a mouse model of CA19-9-positive and CA19-9-negative xenografts with micro-positron emission tomography/micro-computed tomography at successive time intervals after injection. Percentage of injected dose per gram of radioactivity was measured in blood and tumor to provide objective confirmation of the micro-positron emission tomographic images. RESULTS: Tumor xenograft imaging of the anti-CA19-9 cys-diabody demonstrated an average tumor-to-blood ratio of 3.0 and positive-to-negative tumor ratio of 7.4. Successful conjugation of the cys-diabody to PLNs was indicated by flow cytometry showing specific binding of cys-diabody-PLN conjugate to human pancreatic cancer cells in vitro. CONCLUSIONS: Our results show that the anti-CA19-9 cys-diabody targets pancreatic cancer providing specific molecular imaging in tumor xenograft models. Furthermore, the cys-diabody-PLN conjugate demonstrates target-specific binding of human pancreatic cancer cells with the potential to deliver targeted treatment.

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[159]

TÍTULO / TITLE: - The “malignant truth” about the recurrence of pancreatic intraductal papillary mucinous neoplasms-reply.

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

REVISTA / JOURNAL: - Arch Surg. 2012 Oct 1;147(10):977-80. doi: 10.1001/archsurg.2012.2312.

●● Enlace al texto completo (gratuito o de pago)
1001/archsurg.2012.2312
AUTORES / AUTHORS: - Moriya T; Traverso LW

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[160]
TÍTULO / TITLE: - Tumor vessel depiction with contrast-enhanced endoscopic ultrasonography predicts efficacy of chemotherapy in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreas. 2013 Aug;42(6):990-5. doi: 10.1097/MPA.0b013e31827fe94c.
●● Enlace al texto completo (gratuito o de pago)
1097/MPA.0b013e31827fe94c
AUTORES / AUTHORS: - Yamashita Y; Ueda K; Itonaga M; Yoshida T; Maeda H; Maekita T; Iguchi M; Tamai H; Ichinose M; Kato J
INSTITUCIÓN / INSTITUTION: - From the Second Department of Internal Medicine, Wakayama Medical University, Wakayama, Japan.
RESUMEN / SUMMARY: - OBJECTIVES: Contrast-enhanced endoscopic ultrasonography (CE-EUS) is a new imaging modality for pancreatic lesions. The aim of this study was to evaluate if CE-EUS is useful for predicting treatment efficacy before pancreatic cancer chemotherapy by assessing intratumoral vessel flow. METHODS: Thirty-nine patients with unresectable advanced pancreatic cancer underwent CE-EUS before chemotherapy. The patients were divided into 2 groups according to the intratumoral vessel flow observed with CE-EUS: vessel sign-positive and vessel sign-negative groups. Patient prognosis was investigated according to presence or absence of the vessel sign. RESULTS: Two patients were excluded due to poor visualization of CE-EUS images; therefore, 37 patients were analyzed. Contrast-enhanced EUS revealed positive vessel sign in 20 patients, whereas it revealed negative vessel sign in 17 patients. Both progression-free survival and overall survival were significantly longer in the positive- versus negative vessel sign groups (P = 0.037 and P = 0.027, respectively). Multivariate analysis demonstrated that the positive vessel sign was an independent factor associated with longer overall survival (hazard ratio, 0.22; 95% confidence interval, 0.08-0.53). CONCLUSIONS: Evaluation of intratumoral vessel flow by CE-EUS could be useful for predicting efficacy of chemotherapy in patients with pancreatic cancer. Contrast-enhanced EUS could be used before chemotherapy for inoperable pancreatic cancer.

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[161]
TÍTULO / TITLE: - Ectopic pancreas in upper gastrointestinal tract: MRI findings with emphasis on differentiation from submucosal tumor.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Acta Radiol. 2013 Jul 15.

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

1177/0284185113491251

AUTORES / AUTHORS: - Jang KM; Kim SH; Park HJ; Lim S; Kang TW; Lee SJ; Choi D

INSTITUCIÓN / INSTITUTION: - Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - BACKGROUND: Ectopic pancreas can frequently be mistaken for other submucosal masses. Ectopic pancreas may follow the signal intensity of mother pancreas on various magnetic resonance (MR) sequences, which might be helpful for differentiation between ectopic pancreas and other submucosal tumors in upper gastrointestinal (UGI) tract. PURPOSE: To evaluate the value of MR imaging (MRI) in differentiating ectopic pancreases from submucosal tumors in UGI tract. MATERIAL AND METHODS: Fifteen patients with ectopic pancreas and 26 patients with UGI submucosal tumors were included. All patients underwent abdominal MRI with diffusion-weighted imaging (DWI) and gadoxetic acid-enhanced MRI. Qualitative (location, contour, growth pattern, lesion border, and presence of intralesional cystic portion and duct-like structure) and quantitative (long diameter [LD], short diameter [SD], LD/SD ratio, signal intensities and apparent diffusion coefficients [ADC], and signal intensity - and ADC ratios of UGI submucosal lesions to pancreas) parameters were compared between ectopic pancreases and UGI submucosal tumors using Fisher's exact test, the Mann-Whitney U test, and receiver-operating characteristic (ROC) analysis. RESULTS: Duodenum was the most common location for ectopic pancreas (12/15, 79.9%), and the gastric body for UGI submucosal tumors (15/26, 57.7%) (P = 0.005). Round shape was an imaging feature more common in UGI submucosal tumors (12/26, 46.2%) than in ectopic pancreas (1/15, 6.7%; P = 0.021). On all of the various pulse sequences of MR images, ectopic pancreas showed isointensity comparable to that of pancreas more frequently than did sequences of UGI submucosal tumors (P < 0.01).The means (0.95 +/- 0.09, 0.99 +/- 0.06, 1.07 +/- 0.08) of the signal intensity ratio of ectopic pancreas to pancreas on fat-suppressed unenhanced T1-weighted, arterial, and portal phase images were significantly higher than those (0.60 +/- 0.09, 0.62 +/- 0.28, 0.86 +/- 0.27) of UGI submucosal tumors (P < 0.05). In contrast, the means (1.05 +/- 0.12, 0.93 +/- 0.18) of the signal intensity ratios of ectopic pancreas on T2-weighted images and DW images (b = 800 s/mm2) were significantly lower than those (1.82 +/- 0.39, 2.35 +/- 0.94) of UGI submucosal tumors (P < 0.001). On ROC analysis, if absolute value of difference between 1.0 and signal intensity ratio of submucosal lesions to the pancreas on T1-weighted images is <0.21, the sensitivity and specificity reach 100.0% for diagnosis ectopic pancreas from submucosal tumors. CONCLUSION: Abdominal MRI with DWI can be a

valuable tool for differentiating ectopic pancreases from UGI submucosal tumors.

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[162]

TÍTULO / TITLE: - Insulinoma of genetic aetiology.

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

REVISTA / JOURNAL: - Ann Endocrinol (Paris). 2013 Jul;74(3):200-2. doi: 10.1016/j.ando.2013.05.006. Epub 2013 Jun 13.

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

1016/j.ando.2013.05.006

AUTORES / AUTHORS: - Borson-Chazot F; Cardot-Bauters C; Mirallie E; Pattou F

INSTITUCIÓN / INSTITUTION: - Department of endocrinology, hospices civils de Lyon, groupement hospitalier Est, aile A, 59, boulevard Pinel 1, 69677 Bron cedex, France. Electronic address: francoise.borson-chazot@chu-lyon.fr.

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[163]

TÍTULO / TITLE: - A bioengineered metastatic pancreatic tumor model for mechanistic investigation of chemotherapeutic drugs.

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

REVISTA / JOURNAL: - J Biotechnol. 2013 Jul 20;166(4):166-73. doi: 10.1016/j.jbiotec.2013.05.008. Epub 2013 Jun 6.

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

1016/j.jbiotec.2013.05.008

AUTORES / AUTHORS: - Wang X; Zhang X; Fu Z; Yin H

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Bayinguoleng Menggu Zizhizhou People's Hospital, Korla, Xinjiang, China.

RESUMEN / SUMMARY: - Here we bioengineered a metastatic pancreatic tumor model with homogenous human CD133(+)CXCR4(+) cancer stem cells (CSC) and a polyglyconate/gelatin electrospun scaffold. The scaffold sported a highly porous microstructure with the majority of fibers possessing a diameter between 500mum and 1500mum. The scaffold supported the growth of tumor cells without provoking apoptosis. The homogeneous CD133(+)CXCR4(+) CSC was transplanted with the scaffold into the pancreas of nude mice to establish a metastatic pancreatic tumor. After 8 weeks, the tumor volume and weight in the scaffold model were 40.52% and 51.49% greater than the traditional model, respectively. The scaffold also increased the incidence of tumor formation and readily induced a hepatic metastasis. In this model we found that FOLFIRINOX possessed a superior capability of preventing the hepatic metastasis of pancreatic tumor cells than gemcitabine. A mechanistic study attributed this superiority to the fact that FOLFIRINOX could induce a greater apoptosis of CD133(+)CXCR4(+) CSC, thus depriving the driving force of hepatic metastasis. This metastatic tumor model showed an increased incidence of

tumor formation, an accelerated tumorigenesis and a significant hepatic metastasis, therefore offering scientists a proven platform to study chemotherapeutic drugs.

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[164]

TÍTULO / TITLE: - Self-assembling, amphiphilic polymer-gemcitabine conjugate shows enhanced antitumor efficacy against human pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Bioconjug Chem. 2013 Jul 17;24(7):1161-73. doi: 10.1021/bc400032x. Epub 2013 Jun 26.

●● Enlace al texto completo (gratuito o de pago) 1021/bc400032x

AUTORES / AUTHORS: - Chitkara D; Mittal A; Behrman SW; Kumar N; Mahato RI

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical Sciences and double daggerDepartment of Surgery, University of Tennessee Health Science Center , Memphis, Tennessee 38163, United States.

RESUMEN / SUMMARY: - The therapeutic efficacy of gemcitabine is severely compromised due to its rapid plasma metabolism. Moreover, its hydrophilicity poses a challenge for its efficient entrapment in nanosized delivery systems and to provide a sustained release profile. In this study, gemcitabine was covalently conjugated to poly(ethylene glycol)-block-poly(2-methyl-2-carboxyl-propylene carbonate) (PEG-PCC) which could self-assemble into micelles of 23.6 nm. These micelles afforded protection to gemcitabine from plasma metabolism as evident by negligible amount of gemcitabine and its metabolite dFdU detected in the plasma after 24 h. A controlled release of gemcitabine from the micelles was observed with 53.89% drug release in 10 days in the presence of protease enzyme Cathepsin B. Gemcitabine conjugated micelles were cytotoxic, showed internalization, and induced cell apoptosis in MIA PaCa-2 and L3.6pl pancreatic cancer cell lines. These micelles efficiently inhibited tumor growth when injected intravenously into MIA PaCa-2 cell derived xenograft tumor bearing NSG mice at a dose of 40 mg/kg in terms of reduced tumor volume and tumor weight (0.38 g vs 0.58 g). TUNEL assay revealed that gemcitabine conjugated micelles induced a much higher extent of apoptosis in the tumor tissues compared to free gemcitabine. In conclusion, gemcitabine conjugated micelles were able to enhance the drug payload, protect it from rapid plasma metabolism, and provide a sustained release and showed enhanced antitumor activity, and thus have the potential to provide a better therapeutic alternative for treating pancreatic cancer.

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[165]

TÍTULO / TITLE: - Expression of urocortin in pancreatic ductal adenocarcinoma and pancreatic intraepithelial neoplasia.

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

REVISTA / JOURNAL: - APMIS. 2013 Jun 12. doi: 10.1111/apm.12117.

●● Enlace al texto completo (gratuito o de pago) 1111/apm.12117

AUTORES / AUTHORS: - Cheng MF; Tsai WC; Hsia KT; Yang YS; Jin JS

INSTITUCIÓN / INSTITUTION: - Division of Histological and Clinical Pathology, Hualian Army Forces General Hospital, Hualien, Taiwan; Department of Pathology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan; Institute of Oral Biology, School of Dentistry, National Yang-Ming University, Taipei, Taiwan.

RESUMEN / SUMMARY: - Urocortin (UCN) is a 40-aminoacid neuropeptide that regulates angiogenesis and inhibits cell proliferation. Our aim was to examine the relationship of UCN expression to the clinicopathological parameters of pancreatic ductal adenocarcinoma (PDAC) and histological grade of pancreatic intraepithelial neoplasia (PanIN). Tissue microarray was used to analyze UCN protein expression in 89 surgical specimens including 21 PanIN, 3 PDAC arising from PanIN, and 65 PDAC without PanIN. UCN immunoscores ranging from 0 to 12 were obtained by multiplying intensity (scored on a 3-point scale) by the percentage of stained cells (scored on a 4-point scale). Strong expression of UCN was detected in 5 specimens of non-neoplastic pancreatic ductal epithelia. UCN immunoscore was significantly higher in PanIN-1 than in PanIN-2 and PanIN-3 ($p = 0.038$) and significantly higher in well-differentiated PDAC or early American Joint Committee on Cancer (AJCC) stage PDAC than in poorly differentiated or advanced stage PDAC ($p = 0.025$, $p = 0.018$). Higher expression of UCN correlates with PDAC tumor grade and AJCC pathologic stage as well as PanIN grade. Immunohistochemical assessment of UCN may help clinicians predict tumor recurrence rate and help pathologists make a proper diagnosis.

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[166]

TÍTULO / TITLE: - A duodenal duplication cyst manifested by duodenojejunal intussusception and chronic pancreatitis.

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

REVISTA / JOURNAL: - Surgery. 2013 Jun 15. pii: S0039-6060(13)00065-2. doi: 10.1016/j.surg.2013.02.013.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.02.013

AUTORES / AUTHORS: - Kusnierz K; Pilch-Kowalczyk J; Gruszczynska K; Baron J; Lucyga M; Lampe P

INSTITUCIÓN / INSTITUTION: - Department of Gastrointestinal Surgery, Medical University of Silesia, Medykow, Poland. Electronic address: kasiachir@wp.pl.

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[167]

TÍTULO / TITLE: - MAL2 expression predicts distant metastasis and short survival in pancreatic cancer.

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

REVISTA / JOURNAL: - Surgery. 2013 Jul 19. pii: S0039-6060(13)00109-8. doi: 10.1016/j.surg.2013.03.010.

●● Enlace al texto completo (gratuito o de pago) 1016/j.surg.2013.03.010

AUTORES / AUTHORS: - Eguchi D; Ohuchida K; Kozono S; Ikenaga N; Shindo K; Cui L; Fujiwara K; Akagawa S; Ohtsuka T; Takahata S; Tokunaga S; Mizumoto K; Tanaka M

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

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic cancer is associated with a devastating prognosis, partially because of its aggressive metastatic ability. Identification of prognostic markers of metastasis would be useful in the clinical management of postoperative patients with pancreatic cancer. Mal, T-cell differentiation protein 2 (MAL2) has been identified as a molecule predictive of metastases; the clinical relevance of MAL2 in pancreatic cancer is unknown. METHODS: Orthotopic human pancreatic cancer xenografts from the pancreatic cancer cell line SUIT-2 were established in nude mice. Only liver metastasis was harvested and cultured. These metastatic cycles were repeated 5 times to establish a highly metastatic cell line, termed metastatic SUIT-2 (MS). We investigated proliferation and motility of MS cells compared with those of the parent SUIT-2. Microarray analysis was performed to investigate differences in gene expression. We also performed immunohistochemical analysis of 89 formalin-fixed, paraffin-embedded human pancreatic cancer tissue samples to investigate the clinical significance of MAL2 expression. RESULTS: MS cells showed a greater metastatic rate after orthotopic implantation than parental SUIT-2. MS cells had increased motility but decreased proliferation compared with parental SUIT-2. Microarray analyses showed that 26 genes were significantly upregulated (>10-fold) in MS cells compared with parental SUIT-2, particularly MAL2 expression. Immunohistochemical analysis showed that high expression of MAL2 was associated with a lesser survival of postoperative patients (P = .03) and a high rate of distant metastasis (P = .008). CONCLUSION: We characterized a newly established pancreatic cancer cell line with highly metastatic potential. MAL2 is a promising predictive marker for distant metastasis and short survival in patients with resected pancreatic cancer.

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[168]

TÍTULO / TITLE: - Centralization of Services and Reduction of Adverse Events in Pancreatic Cancer Surgery.

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

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

●● Enlace al texto completo (gratuito o de pago) 1007/s00268-013-2108-4

AUTORES / AUTHORS: - Young J; Thompson A; Tait I; Waugh L; McPhillips G

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Ninewells Hospital and Medical School, Dundee, Scotland, UK, jamie.young@nhs.net.

RESUMEN / SUMMARY: - BACKGROUND: The perioperative period is critical in the outcome for patients with pancreatic cancer. The aim of the present analysis was to examine adverse events in patients dying under surgical care in relation to changes in the organization of pancreatic cancer surgery. METHODS: From 1996 to 2005, 1,033 patients with pancreatic cancer, mean age of 71 years (range 21-97 years) died under surgical care. The incidence, mortality, and number of operations for pancreatic cancer remained stable across the time period, but the proportion of patients undergoing surgery in the five specialist cancer centers increased from 50 to 80 % ($p < 0.001$). Prior to death 260 (25 %) patients underwent operation and 96 (9 %) had endoscopic retrograde cholangiopancreatography (ERCP). There was a significant rise in ERCP ($p = 0.03$) and a decrease in non-resectional operations ($p = 0.001$). RESULTS: Since 1996, 52 (15 %) patients in whom 90 adverse events were recorded died following surgical intervention: 28 adverse events related to the perioperative period with 15 due to direct procedure complications such as bleeding or anastomotic leak; 13 were attributed to decision making around the choice or timing of the procedure. The postoperative mortality after curative pancreatic resection reduced from 3.5 to 1.8 %. Identified adverse events fell significantly in patients who died relating to the operative period (median of 3 per annum [1994-2000] to 1 per annum [2001-2005]) ($p = 0.014$) and medical care (3-0) ($p = 0.003$). CONCLUSIONS: Continuous peer review audit has demonstrated a reduction in the number of adverse events in patients dying with pancreatic cancer under surgical care as increased numbers of patients treated in specialist cancer centers.

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[169]

TÍTULO / TITLE: - Suppression of pancreatic tumor growth by targeted arsenic delivery with anti-CD44v6 single chain antibody conjugated nanoparticles.

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

REVISTA / JOURNAL: - Biomaterials. 2013 Aug;34(26):6175-84. doi: 10.1016/j.biomaterials.2013.04.056. Epub 2013 May 27.

●● Enlace al texto completo (gratuito o de pago) 1016/j.biomaterials.2013.04.056

AUTORES / AUTHORS: - Qian C; Wang Y; Chen Y; Zeng L; Zhang Q; Shuai X; Huang K

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou 510120, China.

RESUMEN / SUMMARY: - Arsenic trioxide (As2O3) is a promising anticancer agent for solid tumors. However, the high toxicity to normal tissues resulting from the lack of tumor specificity remains a huge challenge in its systemic application. Targeted vectors enabling drug delivery to specific cancer cells bring about great potential for better therapeutic efficacy whereas low side effects in cancer treatments. Our previous work has demonstrated that the anti-CD44v6 single chain variable fragment (scFv(CD44v6)) screened out from the human phage-displayed scFv library possesses high specificity and affinity to membrane antigen CD44v6 over-expressing in a subset of epithelium-derived cancers, such as pancreatic, hepatocellular, colorectal and gastric cancers. Herein, a maleimide-functionalized amphiphilic diblock copolymer of poly (ethylene glycol) and poly (D, L-lactide) (mal-PEG-PDLLA) was synthesized and assembled to vesicles with arsenite ion (As) encapsulated in their cores (As-NPs). Conjugation of scFv(CD44v6) with mal-PEG-PDLLA (scFv-As-NPs) enabled more efficient delivery of As and exhibited higher cytotoxic activity than non-targeted ones (As-NPs) in human pancreatic cancer cells PANC-1. Furthermore, the targeted delivery of As induced more significant gene suppression in terms of the expression of anti-apoptotic Bcl-2 protein. Consequently, the expression level of cleaved caspase-3 which is a molecular indicator of cell apoptosis was remarkably elevated. In animal tests, scFv-As-NPs were found to greatly increase accumulation of drug in tumor site and potentiate the efficacy of As in inhibiting tumor growth owing to the enhanced cell apoptosis. These results imply that our tumor specific nanocarriers provide a highly efficient and safe platform for pancreatic cancer therapy.

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[170]

TÍTULO / TITLE: - CT-guided radiofrequency ablation following high-dose chemotherapy of a liver-metastasizing pancreatoblastoma with tumor thrombus in the portal vein.

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

REVISTA / JOURNAL: - Pediatr Radiol. 2013 Jul 5.

●● Enlace al texto completo (gratuito o de pago) 1007/s00247-013-2698-x

AUTORES / AUTHORS: - Zheng J; Zhang H; Sun Y; Sun B

INSTITUCIÓN / INSTITUTION: - Center of Minimally Invasive Intervention, Beijing You-an Hospital, Capital Medical University, Beijing, 100069, People's Republic of China, jiashengzheng@yahoo.com.

RESUMEN / SUMMARY: - Pancreatoblastoma is a rare neoplasm encountered most commonly in infants and young children. Unresectable or metastatic tumors have a poor prognosis despite adjuvant chemotherapy or radiotherapy. We report the successful use of CT-guided radiofrequency ablation subsequent to intensive chemotherapy in an 8-year-old girl with liver-metastasizing

pancreatoblastoma and with right and segment 4 portal vein tumor thrombosis. She has been in remission for 3 years.

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[171]

TÍTULO / TITLE: - Pim-3 promotes the growth of human pancreatic cancer in the orthotopic nude mouse model through vascular endothelium growth factor.

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

REVISTA / JOURNAL: - J Surg Res. 2013 Jun 28. pii: S0022-4804(13)00593-3. doi: 10.1016/j.jss.2013.06.004.

●● Enlace al texto completo (gratuito o de pago) 1016/j.jss.2013.06.004

AUTORES / AUTHORS: - Wang C; Li HY; Liu B; Huang S; Wu L; Li YY

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

RESUMEN / SUMMARY: - BACKGROUND: As one of the most lethal cancers, pancreatic cancer presents poor prognosis with an overall 5-y survival of less than 5%. We previously reported that Pim-3, a member of the proto-oncogene Pim family that encodes serine/threonine kinases, is aberrantly expressed in human pancreatic cancer lesions. In the current study, we investigated the role of Pim-3 in promoting tumor growth and angiogenesis in an orthotopic nude mouse model of human pancreatic cancer. METHODS: We constructed retroviral vectors for human Pim-3 and a kinase-dead mutant of human Pim-3 (K69M); the retroviral supernatants generated from these vectors were then used to infect the human pancreatic cancer cell line MiaPaCa-2 to establish stable cell lines. We assessed cell proliferation using CCK-8, tumor growth, and angiogenesis in vivo in an orthotopic mouse model of pancreatic cancer. While tumor size was measured using magnetic resonance imaging, the tumor tissues were excised for protein extraction and histological analysis to detect vascular endothelium growth factor (VEGF) expression and vessel density. RESULTS: We established an orthotopic nude mouse model of human pancreatic cancer. We observed that Pim-3 promoted the proliferation of human pancreatic cancer cells, both in vitro and in vivo. Moreover, Pim-3 is required for vasculogenesis of primary human pancreatic tumors in vivo and promotion of angiogenesis through the induction of VEGF expression. CONCLUSIONS: Pim-3 can promote tumor growth and angiogenesis by stimulating the VEGF pathway.

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[172]

TÍTULO / TITLE: - A randomized controlled trial of a cardiopulmonary resuscitation video in advance care planning for progressive pancreas and hepatobiliary cancer patients.

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

REVISTA / JOURNAL: - J Palliat Med. 2013 Jun;16(6):623-31. doi: 10.1089/jpm.2012.0524. Epub 2013 Apr 22.

●● Enlace al texto completo (gratuito o de pago) 1089/jpm.2012.0524

AUTORES / AUTHORS: - Epstein AS; Volandes AE; Chen LY; Gary KA; Li Y; Agre P; Levin TT; Reidy DL; Meng RD; Segal NH; Yu KH; Abou-Alfa GK; Janjigian YY; Kelsen DP; O'Reilly EM

INSTITUCIÓN / INSTITUTION: - Memorial Sloan-Kettering Cancer Center, New York, New York, USA. epsteina@mskcc.org

RESUMEN / SUMMARY: - BACKGROUND: Cardiopulmonary resuscitation (CPR) is an important advance directive (AD) topic in patients with progressive cancer; however such discussions are challenging. OBJECTIVE: This study investigates whether video educational information about CPR engenders broader advance care planning (ACP) discourse. METHODS: Patients with progressive pancreas or hepatobiliary cancer were randomized to an educational CPR video or a similar CPR narrative. The primary end-point was the difference in ACP documentation one month posttest between arms. Secondary end-points included study impressions; pre- and post-intervention knowledge of and preferences for CPR and mechanical ventilation; and longitudinal patient outcomes. RESULTS: Fifty-six subjects were consented and analyzed. Rates of ACP documentation (either formal ADs or documented discussions) were 40% in the video arm (12/30) compared to 15% in the narrative arm (4/26), OR=3.6 [95% CI: 0.9-18.0], p=0.07. Post-intervention knowledge was higher in both arms. Posttest, preferences for CPR had changed in the video arm but not in the narrative arm. Preferences regarding mechanical ventilation did not change in either arm. The majority of subjects in both arms reported the information as helpful and comfortable to discuss, and they recommended it to others. More deaths occurred in the video arm compared to the narrative arm, and more subjects died in hospice settings in the video arm. CONCLUSIONS: This pilot randomized trial addressing downstream ACP effects of video versus narrative decision tools demonstrated a trend towards more ACP documentation in video subjects. This trend, as well as other video effects, is the subject of ongoing study.

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[173]

TÍTULO / TITLE: - CEACAM6 induces epithelial-mesenchymal transition and mediates invasion and metastasis in pancreatic cancer.

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

REVISTA / JOURNAL: - Int J Oncol. 2013 Sep;43(3):877-85. doi: 10.3892/ijo.2013.2015. Epub 2013 Jul 12.

●● Enlace al texto completo (gratuito o de pago) 3892/ijo.2013.2015

AUTORES / AUTHORS: - Chen J; Li Q; An Y; Lv N; Xue X; Wei J; Jiang K; Wu J; Gao W; Qian Z; Dai C; Xu Z; Miao Y

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, The First Affiliated Hospital of Nanjing Medical University, Nanjing, P.R. China.

RESUMEN / SUMMARY: - Pancreatic cancer is a disease with an extremely poor prognosis. The acquisition of invasion properties in pancreatic cancer is accompanied by the process of epithelial-mesenchymal transition (EMT). Carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6) is emerging as an important determinant of the malignant phenotype in a range of cancers, including pancreatic cancer. Therefore, the aim of this study was to evaluate the potential involvement of CEACAM6 in the invasion and metastasis of pancreatic cancer cells via EMT regulation. The results of our study showed a positive association between CEACAM6 expression and poor prognosis of pancreatic cancer, differentiation and lymph node metastasis. Elevated levels of CEACAM6 in pancreatic cancer cells promoted EMT, migration and invasion in vitro and metastasis in animal models, whereas shRNA-mediated CEACAM6 knockdown had the opposite effect. Furthermore, we demonstrated that miR-29ª/b/c specific for CEACAM6 could regulate its expression at the post-transcriptional level. Collectively, our findings identified CEACAM6, which is regulated by miR-29ª/b/c, as an important positive regulator of EMT in pancreatic cancer offering an explanation for how elevated levels of CEACAM6 are likely to contribute to the highly metastatic phenotype of pancreatic cancer.

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[174]

TÍTULO / TITLE: - Immature squamous metaplasia (focal atypical epithelial hyperplasia) of the pancreatic duct-immunohistochemical distinction from intraductal carcinoma.

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

REVISTA / JOURNAL: - Histopathology. 2013 May 3. doi: 10.1111/his.12180.

●● Enlace al texto completo (gratuito o de pago) 1111/his.12180

AUTORES / AUTHORS: - Mochizuki K; Kondo T; Oishi N; Kawasaki T; Nakazawa T; Yamane T; Katoh R

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, Yamanashi, Japan.

RESUMEN / SUMMARY: - AIMS: Immature squamous metaplasia of the pancreatic duct (ISMPD) can be difficult to differentiate from an intraductal carcinoma of the pancreas (ICP), and little is known about the pathological nature of ISMPD. The aim of this study was to analyse 20 ISMPD and 10 ICP tissue samples. METHODS AND RESULTS: ISMPD shares some characteristics with ICP. Seven of 20 ISMPD samples were covered by a layer of pancreatic duct epithelium, whereas this was not seen in the ICP samples. Immunohistochemistry of ISMPD revealed positivity for p63 (100%), cytokeratin 5/6 (95%), cytokeratin 7 (95%), cytokeratin 20 (10%), and MUC-1 (95%), and the samples were negative for p53, carcinoembryonic antigen (CEA), and bcl-2.

In contrast, ICP was positive for p63 (40%), p53 (10%), cytokeratin 7 (90%), cytokeratin 20 (20%), CEA (30%), and MUC-1 (80%), and negative for cytokeratin 5/6. However, in 84% (16) of the ISMPD samples, cytokeratin 7 was expressed only by an epithelial layer at the apical surface; this expression pattern was not found in any of the 10 ICP samples. The mean Ki67 labelling index was 1.0% in ISMPD and 18.5% in ICP. CONCLUSIONS: Our study suggests that immunohistochemical staining for cytokeratin 5/6 and Ki67 constitutes the best combination for differentiating ISMPD from ICP.

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[175]

TÍTULO / TITLE: - Animal models and cell lines of pancreatic neuronimal models and cell lines of pancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - Pancreas. 2013 Aug;42(6):912-23. doi: 10.1097/MPA.0b013e31827ae993.

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

1097/MPA.0b013e31827ae993

AUTORES / AUTHORS: - Babu V; Paul N; Yu R

INSTITUCIÓN / INSTITUTION: - From the Divisions of *Endocrinology and daggerGastroenterology, Cedars-Sinai Medical Center, Los Angeles, CA.

RESUMEN / SUMMARY: - Pancreatic neuroendocrine tumors (PNETs), also known as islet cell tumors, are mostly indolent neoplasms that probably arise from a network of endocrine cells that includes islet cells and pluripotent precursors in the pancreatic ductal epithelium. The incidence and prevalence of PNETs continue to rise in recent years because of more sensitive detection. The molecular pathogenesis, early detection, molecular predictors of tumor behavior, and targeted drug therapy of PNETs are not well understood and require additional basic and translational research. The rarity and indolent nature of these tumors, difficulty of access to appropriate patient tissue samples, and varying histopathology and secreted hormones pose particular challenges to PNET researchers. Animal models and cell lines are indispensable tools for investigating the pathogenesis, pathophysiology, mechanisms for tumor invasion and metastasis, and therapeutics of PNETs. This review summarizes currently available animal models and cell lines of PNETs, which have provided valuable insights into the pathogenesis and natural history of human PNETs. In the future, animal models and cell lines of PNETs should also be used to study early tumor detection and molecular predictors of tumor behavior and to test the responses to, and mechanisms for, novel targeted drug therapies.

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[176]

TÍTULO / TITLE: - Metastatic Renal Cell Carcinoma to the Pancreas: Diagnostic Significance of Fine-Needle Aspiration Cytology.

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

REVISTA / JOURNAL: - Acta Cytol. 2013 Jul 12;57(4):418-422.

●● Enlace al texto completo (gratuito o de pago) 1159/000351299

AUTORES / AUTHORS: - Gilani SM; Tashjian R; Danforth R; Fathallah L

INSTITUCIÓN / INSTITUTION: - Department of Pathology, St. John Hospital and Medical Center, Detroit, Mich., USA.

RESUMEN / SUMMARY: - Background: Renal cell carcinoma rarely metastasizes to the pancreas. Diagnosing a neoplasm that is metastatic to the pancreas by fine-needle aspiration (FNA) cytology is often challenging. A detailed clinical history may prove to be beneficial. Case Reports: A total of 729 pancreatic FNAs were performed from January 2005 through August 2012 at our institution. Among these, we found 3 patients with a prior history of a malignant renal neoplasm who presented with a pancreatic mass: 2 in the tail and 1 in the head. Radiographically, they ranged in size from 2.5 to 7.0 cm. Microscopic evaluation of cytologic material obtained during endoscopic ultrasound-guided FNA (EUS-FNA) revealed cohesive clusters of atypical cells with clear cytoplasm and prominent nucleoli surrounded by a thin capillary network. The neoplastic cells were immunoreactive with CD10 (cases 2 and 3). A diagnosis of metastatic clear cell renal cell carcinoma was rendered for each case based on the morphologic features and immunohistochemical staining pattern of the neoplastic cells. Histologic comparison with the available slides of the corresponding primary renal neoplasm confirmed the diagnosis. Conclusion: We conclude that EUS-FNA of pancreatic masses is an important, effective, and accurate diagnostic modality for early diagnosis of both primary and metastatic neoplasms of the pancreas.

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[177]

TÍTULO / TITLE: - Pancreatic involvement in neuroblastoma with radiologic-pathologic correlation: a single-institution experience.

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

REVISTA / JOURNAL: - AJR Am J Roentgenol. 2013 Jul;201(1):W141-6. doi: 10.2214/AJR.12.9618.

●● Enlace al texto completo (gratuito o de pago) 2214/AJR.12.9618

AUTORES / AUTHORS: - Rosenbaum DG; Abramson SJ; Delappe E; Teruya-Feldstein J; La Quaglia MP; Fox JJ; Price AP

INSTITUCIÓN / INSTITUTION: - 1 Department of Radiology, New York-Presbyterian Hospital and Weill Cornell Medical Center, 525 E 68th St, Box 141, New York, NY 10065.

RESUMEN / SUMMARY: - OBJECTIVE. Pancreatic involvement in neuroblastoma is extremely rare, with few cases reported in the literature. We present imaging findings of pancreatic involvement in neuroblastoma with clinical and pathologic

correlation in the largest documented series to date. SUBJECTS AND METHODS. We prospectively reported pancreatic involvement evident on multimodality imaging in neuroblastoma patients presenting to our institution from 1997 to 2011. Lesions were classified according to location within the pancreas, and imaging features were correlated with cytogenetic and surgicopathologic findings. RESULTS. Neuroblastoma involving the pancreas was evident on imaging of seven of 1031 patients (mean age, 6.6 years). One patient had pancreatic involvement at presentation, and six developed pancreatic disease at relapse or disease progression. Pancreatic lesions were most frequently initially identified on concurrent CT and (123)I-metaiodobenzylguanidine scintigraphy, and additional lesions initially were found on MRI and ultrasound. Five of seven patients had focal lesions, one had diffuse pancreatic involvement, and one had pancreatic extension from contiguous disease. The distribution of lesions favored the pancreatic body and tail. All patients had International Neuroblastoma Staging System stage 3 or 4 disease, Children's Oncology Group intermediate- or high-risk disease, and unfavorable histology at initial diagnosis. For the five patients with surgical correlation, pancreatic surgical specimens revealed neuroblastoma in three cases and ganglioneuroblastoma in two cases. CONCLUSION. Although rare, pancreatic involvement in neuroblastoma occurs. Its variable imaging appearance should be considered when evaluating the retroperitoneum in patients with known or suspected neuroblastoma, particularly because increased patient survival holds the potential for uncommon patterns of recurrence.

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[178]

TÍTULO / TITLE: - Metabonomic studies of pancreatic cancer response to radiotherapy in a mouse xenograft model using magnetic resonance spectroscopy and principal components analysis.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Jul 14;19(26):4200-8. doi: 10.3748/wjg.v19.i26.4200.

●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i26.4200

AUTORES / AUTHORS: - He XH; Li WT; Gu YJ; Yang BF; Deng HW; Yu YH; Peng WJ

INSTITUCIÓN / INSTITUTION: - Xin-Hong He, Wen-Tao Li, Ya-Jia Gu, Bao-Feng Yang, Wei-Jun Peng, Department of Radiology, Fudan University Shanghai Cancer Center, Shanghai 200032, China.

RESUMEN / SUMMARY: - AIM: To investigate the metabolic profiles of xenograft pancreatic cancer before and after radiotherapy by high-resolution magic angle spinning proton magnetic resonance spectroscopy (HRMAS (1)H NMR) combined with principal components analysis (PCA) and evaluate the radiotherapeutic effect. METHODS: The nude mouse xenograft model of

human pancreatic cancer was established by injecting human pancreatic cancer cell SW1990 subcutaneously into the nude mice. When the tumors volume reached 800 mm(3), the mice received various radiation doses. Two weeks later, tumor tissue sections were prepared for running the NMR measurements. (1)H NMR and PCA were used to determine the changes in the metabolic profiles of tumor tissues after radiotherapy. Metabolic profiles of normal pancreas, pancreatic tumor tissues, and radiation- treated pancreatic tumor tissues were compared. RESULTS: Compared with (1)H NMR spectra of the normal nude mouse pancreas, the levels of choline, taurine, alanine, isoleucine, leucine, valine, lactate, and glutamic acid of the pancreatic cancer group were increased, whereas an opposite trend for phosphocholine, glycerophosphocholine, and betaine was observed. The ratio of phosphocholine to creatine, and glycerophosphocholine to creatine showed noticeable decrease in the pancreatic cancer group. After further evaluation of the tissue metabolic profile after treatment with three different radiation doses, no significant change in metabolites was observed in the (1)H NMR spectra, while the inhibition of tumor growth was in proportion to the radiation doses. However, PCA results showed that the levels of choline and betaine were decreased with the increased radiation dose, and conversely, the level of acetic acid was dramatically increased. CONCLUSION: The combined methods were demonstrated to have the potential for allowing early diagnosis and assessment of pancreatic cancer response to radiotherapy.

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[179]

TÍTULO / TITLE: - Body Mass Index, Cholecystitis, Cholelithiasis, Pancreatitis and Imaging of Common Bile Duct Stones.

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

REVISTA / JOURNAL: - Am J Med Sci. 2013 Jul 8.

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

1097/MAJ.0b013e318296a6fe

AUTORES / AUTHORS: - Coban G; Yldrm E; Gokturk S; Calskan Z; Turk E; Akcil M

INSTITUCIÓN / INSTITUTION: - Departments of Radiology (GC, EY), Gastroenterology (SG, ZC), and General Surgery (ET), Baskent University Faculty of Medicine, Konya; and Department of Statistics and Computer Science (MA), Baskent University Faculty of Science and Letters, Ankara, Turkey.

RESUMEN / SUMMARY: - PURPOSE:: Studies to date have not investigated whether body mass index (BMI) affects the sensitivity and specificity of magnetic resonance cholangiopancreatography (MRCP). The purpose of this study was to investigate the effect of BMI and also concomitant pancreatitis, cholecystitis and cholelithiasis on the sensitivity and specificity of MRCP. MATERIALS AND METHODS:: Between January 2004 and December 2011,

185 patients were included in the study and divided into 3 groups according to BMI as normal, overweight or obese. Both MRCP and endoscopic retrograde cholangiopancreatography (ERCP) were performed in all patients. ERCP was accepted as the “gold standard.” The accuracy, sensitivity and specificity values of the 3 groups were calculated to determine any effects on the results of the MRCP. RESULTS:: Before separating into groups according to BMI, the statistical results for MRCP in the detection of stone disease were as follows: specificity 74.3%, sensitivity 81.7% and accuracy 79%. After dividing the patients into 3 groups according to BMI, the specificity of stone detection with MRCP in the normal-weight group was 93.8% but decreased to 65.5% in the overweight group and to 72% in the obese group. The sensitivity of stone detection with MRCP in the normal-weight group was 85.2% but decreased to 75% in the overweight group and increased to 88.9% in the obese group. The accuracy was 88.3% in the normal-weight group but decreased to 71.6% in the overweight group and to 81.9% in the obese group. CONCLUSION:: Our study showed that MRCP performance was decreased in the overweight and obese groups.

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[180]

TÍTULO / TITLE: - Andrographolide causes apoptosis via inactivation of STAT3 and Akt and potentiates antitumor activity of gemcitabine in pancreatic cancer.

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

REVISTA / JOURNAL: - Toxicol Lett. 2013 Jul 8;222(1):23-35. doi: 10.1016/j.toxlet.2013.06.241.

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

1016/j.toxlet.2013.06.241

AUTORES / AUTHORS: - Bao GQ; Shen BY; Pan CP; Zhang YJ; Shi MM; Peng CH

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Ruijin Hospital, Shanghai Jiao Tong University School of medicine (SJTU-SM), Shanghai 200025, PR China.

RESUMEN / SUMMARY: - Gemcitabine is a first-line drug utilised in the chemotherapy of pancreatic cancer; however, this drug induces chemo-resistance and toxicity to normal tissue during treatment. Here, we firstly report that andrographolide (ANDRO) alone not only has anti-pancreatic cancer activity, but it also potentiates the anti-tumour activity of gemcitabine. Treatment with ANDRO alone inhibits proliferation of the pancreatic cancer cell lines in a dose- and time-dependent manner in vitro. Interestingly, ANDRO induces cell cycle arrest and apoptosis of pancreatic cancer cells by inhibiting STAT3 and Akt activation, upregulating the expression of p21WAF1 and Bax, and downregulating the expression of cyclinD1, cyclinE, survivin, X-IAP and Bcl-2. Additionally, ANDRO combined with gemcitabine significantly induce stronger cell cycle arrest and more obvious apoptosis than each single treatment. The

mechanistic study demonstrates that this synergistic effect is also dependent on the inhibition of STAT3 and Akt activations which subsequently regulates the pathways involved in the apoptosis and cell cycle arrest. Furthermore, both ANDRO alone and the combination treatments exhibit efficacious anti-tumour activity in vivo. Overall, our results provide solid evidence supporting that ANDRO alone or its combination with gemcitabine is a potential chemotherapeutic approach for treating human pancreatic cancer in clinical practice.

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[181]

TÍTULO / TITLE: - Retrospective analysis of 102 cases of solid pseudopapillary neoplasm of the pancreas in China.

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

REVISTA / JOURNAL: - J Int Med Res. 2013 Aug;41(4):1266-71. doi: 10.1177/0300060513488516. Epub 2013 Jun 27.

●● Enlace al texto completo (gratuito o de pago) 1177/0300060513488516

AUTORES / AUTHORS: - Wang LJ; Bai L; Su D; Zhang TT; Mao ZY; Guo XC; Jiao SC

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Chinese People's Liberation Army General Hospital, PLA Medical School, Beijing, China.

RESUMEN / SUMMARY: - OBJECTIVE: Clinicopathological features and surgical outcomes in patients with solid pseudopapillary neoplasm (SPN) of the pancreas were analysed. METHODS: Data regarding clinicopathological features, surgery and outcome for patients with SPN were retrospectively collected and analysed. Patients were followed-up by telephone interview. RESULTS: The study included 102 patients (89 females/13 males), 99 of whom underwent surgical resection. A total of 89 patients (87.3%) were followed-up (mean duration 26.98 months, range 2-95 months); 86 (96.6%) had no relapse or metastasis. CONCLUSIONS: Surgical resection is the primary therapy for SPN, and results in a good prognosis.

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[182]

TÍTULO / TITLE: - Antiangiogenic effects of oxymatrine on pancreatic cancer by inhibition of the NF-kappaB-mediated VEGF signaling pathway.

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

REVISTA / JOURNAL: - Oncol Rep. 2013 Aug;30(2):589-95. doi: 10.3892/or.2013.2529. Epub 2013 Jun 7.

●● Enlace al texto completo (gratuito o de pago) 3892/or.2013.2529

AUTORES / AUTHORS: - Chen H; Zhang J; Luo J; Lai F; Wang Z; Tong H; Lu D; Bu H; Zhang R; Lin S

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary-Pancreatic Surgery, The Second Affiliated Hospital of Wenzhou Medical College, Wenzhou, Zhejiang 325027, P.R. China.

RESUMEN / SUMMARY: - Oxymatrine, the main alkaloid component in the traditional Chinese herbal medicine Sophora japonica (Sophora flavescens Ait), has been reported to have antitumor properties. However, the mechanisms of action in human pancreatic cancer are not well established to date. In the present study, we investigated the antiangiogenic effects of oxymatrine on human pancreatic cancer as well as the possible mechanisms involved. The results of the cell viability assay showed that treatment of PANC-1 pancreatic cancer cells with oxymatrine resulted in cell growth inhibition in a dose- and time-dependent manner. To investigate the possible mechanisms involved in these events, we performed western blotting and reverse transcription-polymerase chain reaction (RT-PCR) analysis. The results revealed that oxymatrine decreased the expression of angiogenesis-associated factors, including nuclear factor kappaB (NF-kappaB) and vascular endothelial growth factor (VEGF). Finally, the antiproliferative and antiangiogenic effects of oxymatrine on human pancreatic cancer were further confirmed in pancreatic cancer xenograft tumors in nude mice. In conclusion, our studies for the first time suggest that oxymatrine has potential antitumor effects on pancreatic cancer via suppression of angiogenesis, probably through regulation of the expression of the NF-kappaB-mediated VEGF signaling pathway.

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[183]

TÍTULO / TITLE: - Regulation of miR-155 affects pancreatic cancer cell invasiveness and migration by modulating the STAT3 signaling pathway through SOCS1.

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

REVISTA / JOURNAL: - Oncol Rep. 2013 Jun 28. doi: 10.3892/or.2013.2576.

●● Enlace al texto completo (gratuito o de pago) 3892/or.2013.2576

AUTORES / AUTHORS: - Huang C; Li H; Wu W; Jiang T; Qiu Z

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Affiliated First People's Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200080, P.R. China.

RESUMEN / SUMMARY: - In the present study, we investigated the effects of miR-155 on pancreatic cancer cell invasion and migration in vitro, underlying gene expression, expression of miR-155 and its target genes in pancreatic cancer tissues, and their association with metastasis and clinical stage. miR-155 mimics and an inhibitor were transfected into Panc-1 and Capan-2 cells in order to regulate the expression of miR-155. qPCR and western immunoblotting were performed in order to detect gene expression. Transwell assays were performed to characterize the invasion and migration of pancreatic cancer cells in vitro. Immunohistochemical analysis and in situ hybridization were used to

detect the expression of protein and microRNA in pancreatic cancer tissue. miR-155 mimics and an inhibitor upregulated and downregulated, respectively, the expression of miR-155 in pancreatic cancer cells. The invasion and migration of pancreatic cancer cells increased or decreased along with miR-155 expression in vitro. Suppressor of cytokine signaling 1 (SOCS1) protein expression was upregulated when miR-155 was inhibited and downregulated when miR-155 was increased. However, the expression of P-signal transducer and activator of transcription-3 (STAT3) was synchronized with that of miR-155. Transcription of SOCS1 and STAT3 was unchanged by miR-155 regulation. miR-155 expression was high in pancreatic cancer tissues and SOCS1 expression was high in tumor-adjacent tissues. There was no relationship between these genes in cancer and tumor-adjacent tissues. In addition, miR-155 expression was associated with lymph node metastasis and clinical stage. In conclusion, miR-155 plays an important role in the regulation of pancreatic cancer cell invasion and migration by modulating the STAT3 signaling pathway and reducing SOCS1 expression in pancreatic cancer cells.

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[184]

TÍTULO / TITLE: - The microRNA-218 and ROBO-1 signaling axis correlates with the lymphatic metastasis of pancreatic cancer.

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

REVISTA / JOURNAL: - Oncol Rep. 2013 Aug;30(2):651-8. doi: 10.3892/or.2013.2516. Epub 2013 Jun 3.

●● Enlace al texto completo (gratuito o de pago) 3892/or.2013.2516

AUTORES / AUTHORS: - He H; Di Y; Liang M; Yang F; Yao L; Hao S; Li J; Jiang Y; Jin C; Fu D

INSTITUCIÓN / INSTITUTION: - Pancreatic Disease Institute, Department of Pancreatic Surgery, Huashan Hospital, Fudan University, Shanghai 200040, P.R. China.

RESUMEN / SUMMARY: - Pancreatic cancer is known for its poor prognosis and early lymphatic metastasis is a notable characteristic. microRNAs (miRNAs) have been shown to be involved in the initiation and progression of pancreatic cancer. We, therefore, established a screening strategy to find miRNAs related to the lymphatic metastasis of pancreatic cancer and explored the target genes of miRNAs. miRNA array profiles were analyzed in tissue samples [pancreatic ductal adenocarcinoma (PDAC) and matched adjacent benign tissues (MAT)] and cell lines (BxPC-3-LN and BxPC-3). Combined analysis of profiling data from tissue samples and cell lines was used to identify miRNAs related to the lymphatic metastasis of pancreatic cancer. The expression levels of miRNAs were confirmed by realtime reverse transcription PCR (RT-PCR) in tissue samples and cell lines. The correlation between miRNAs and clinicopathological characteristics was investigated. The expression features of miRNAs in pancreatic cancer, precursor lesions and metastatic lymph nodes were

characterized by in situ hybridization (ISH). Predicted target genes of miRNAs were validated by RT-PCR and the protein levels of target genes were revealed by western blotting. Seventy and 63 miRNAs were differentially expressed in pancreatic cancer and BxPC-3-LN, compared to MAT and BxPC-3, respectively. Combined microarray analysis found 4 co-differentially expressed miRNAs (miRNA-663, miRNA-145, miRNA-218 and let-7) related to the lymphatic metastasis of pancreatic cancer. miRNA-218 was significantly downregulated in BxPC-3-LN (fold-change >10) and the expression levels of miRNA-218 were confirmed by RT-PCR. The group with lymph node metastasis and the elder group (age >64) showed lower expression of miRNA-218 (P=0.003 and 0.002), compared to patients without lymph nodes metastasis and patients in the younger group (age </=64), respectively. The expression of miRNA218 showed a decreasing trend from normal acinar/ductal epithelium, intraductal papillary mucinous neoplasm (IPMN), pancreatic cancer to metastatic lymph nodes by ISH. Among 8 predicted target genes of miRNA-218, rodent bone (ROBO-1) was confirmed to be upregulated in both mRNA and protein levels in pancreatic cancer. In conclusion, we established a screening strategy based on microarray results and found miRNA-218 to be a notable gene related to lymphatic metastasis of pancreatic cancer. Downregulation of miRNA-218 and upregulation of ROBO-1 were first demonstrated in pancreatic cancer. The miRNA-218 and ROBO-1 signaling axis may contribute to the lymphatic metastasis of pancreatic cancer.

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[185]

TÍTULO / TITLE: - Feasibility and efficacy of combined cisplatin plus irinotecan chemotherapy for gastroenteropancreatic neuroendocrine carcinomas.

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

REVISTA / JOURNAL: - Med Oncol. 2013 Sep;30(3):664. doi: 10.1007/s12032-013-0664-y. Epub 2013 Jul 18.

●● Enlace al texto completo (gratuito o de pago) 1007/s12032-013-0664-y

AUTORES / AUTHORS: - Lu ZH; Li J; Lu M; Zhang XT; Li J; Zhou J; Wang XC; Gong JF; Gao J; Li Y; Shen L

INSTITUCIÓN / INSTITUTION: - Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of GI Oncology, Peking University School of Oncology, Beijing Cancer Hospital and Institute, Beijing 100142, China.

RESUMEN / SUMMARY: - No standard treatment is currently available for gastroenteropancreatic neuroendocrine carcinomas (GEP-NEC). Therefore, we conducted this study to evaluate the effect of the combination of irinotecan and cisplatin in the treatment of GEP-NECs. Clinical data of 16 locally advanced or metastatic GEP-NEC patients treated with irinotecan plus cisplatin regimen in our center from September 2009 to August 2011 were reviewed. The regimen

included 2-week cycles of 180 mg/m(2) irinotecan and 50 mg/m(2) cisplatin on day 1. Median age was 57 years. The overall response rate was 57.1%, with a disease control rate of 78.6%. One patient achieved pathologic complete response and underwent esophagectomy after chemotherapy. Two patients who had gotten progressive disease were given sequential octreotide long-acting release (LAR) treatment and got disease progression again within 1 month. Six patients who achieved disease control received octreotide LAR as maintenance treatment. The total number of cycles of octreotide was 41, with a median of 4.5 (3-20 cycles). The progression-free survival was 5.5 months, with overall survival of 10.6 months. Grades 3-4 hematological adverse events (AEs) occurred in 10 patients (62.5%) and 3 patients (18.7%) suffered grades 3-4 non-hematological AEs; no patient died of AEs. The irinotecan plus cisplatin chemotherapy is moderately effective and tolerable well tolerated in advanced or metastatic GEP-NEC patients; octreotide LAR may be a good maintenance treatment and should be considered as a treatment option for these patients in the future.

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[186]

TÍTULO / TITLE: - Inflammatory cytokines in human pancreatic cancer.

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

REVISTA / JOURNAL: - Cancer Lett. 2013 Jul 20. pii: S0304-3835(13)00534-X. doi: 10.1016/j.canlet.2013.07.014.

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

1016/j.canlet.2013.07.014

AUTORES / AUTHORS: - Roshani R; McCarthy F; Hagemann T

INSTITUCIÓN / INSTITUTION: - Centre for Cancer and Inflammation, Barts Cancer Institute, Queen Mary, University of London, John Vane Science Centre, Charterhouse Square, London EC1M 6BQ, UK. Electronic address: r.roshani@qmul.ac.uk.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal types of cancer with poor prognosis. Despite extensive efforts, the current treatment methods have limited success. Therefore, novel therapeutic approaches are required. The pancreatic tumor microenvironment is rich in growth factors and inflammatory cytokines that support tumor growth, and it is highly immunosuppressive. Up-regulation of cytokine pathways has been shown to modulate PDAC progression and immune evasion; therefore targeting cytokines may have therapeutic benefits. In this review we provide an overview of current understanding of pro- and anti-inflammatory cytokines in pancreatic cancer and their potential as therapeutic targets.

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[187]

TÍTULO / TITLE: - Complete pancreas divisum with patulous minor papilla complicated by multifocal branch-duct intraductal papillary mucinous neoplasms.

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

REVISTA / JOURNAL: - Endoscopy. 2013;45 Suppl 2 UCTN:E199-200. doi: 10.1055/s-0033-1344160. Epub 2013 Jul 5.

●● Enlace al texto completo (gratuito o de pago) 1055/s-0033-1344160

AUTORES / AUTHORS: - Nakagawa Y; Yamauchi M; Ogawa R; Watada M; Mizukami K; Okimoto T; Kodama M; Murakami K; Fujioka T

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Faculty of Medicine, Oita University, Yufu, Japan. nakagawa4423@ybb.ne.jp

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[188]

TÍTULO / TITLE: - LAMC2: A promising new pancreatic cancer biomarker identified by proteomic analysis of pancreatic adenocarcinoma tissues.

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

REVISTA / JOURNAL: - Mol Cell Proteomics. 2013 Jun 24.

●● Enlace al texto completo (gratuito o de pago) 1074/mcp.M112.023507

AUTORES / AUTHORS: - Kosanam H; Prassas I; Chrystoja CC; Soleas I; Chan A; Dimitromanolakis A; Blasutig IM; Ruckert F; Gruetzmann R; Pilarsky C; Maekawa M; Brand R; Diamandis EP

INSTITUCIÓN / INSTITUTION: - University Health Network, Canada;

RESUMEN / SUMMARY: - In pancreatic cancer, the incidence and mortality curves coincide. One major reason for this high mortality rate in pancreatic ductal adenocarcinoma (PDAC) patients is the dearth of effective diagnostic, prognostic and disease-monitoring biomarkers. Unfortunately, existing tumor markers, as well as current imaging modalities, are not sufficiently sensitive and/or specific for early-stage diagnosis. There is, therefore, an urgent need for improved serum markers of the disease. Herein, we performed Orbitrap mass spectrometry proteomic analysis of four PDAC tissues and their adjacent benign tissues and identified a total of 2,190 non-redundant proteins. Sixteen promising candidates were selected for further scrutiny using a systematic scoring algorithm. Our preliminary serum verification of the top four candidates (DSP, LAMC2, GP73, and DSG2) in 20 patients diagnosed with pancreatic cancer and 20 with benign pancreatic cysts, showed a significant ($p<0.05$) elevation of LAMC2 in pancreatic cancer serum. Extensive validation of LAMC2 in healthy, benign, and PDAC sera from geographically diverse cohorts (n=425) (Japan, Europe, and USA) demonstrated a significant increase in levels in early-stage PDAC compared to benign diseases. The sensitivity of LAMC2 was comparable to CA19.9 in all datasets, with an AUC value greater than 0.85 in discriminating healthy patients from early-stage PDAC patients. The combination of LAMC2 and CA19.9 improved the individual diagnostic performance of CA19.9 in distinguishing healthy and benign subjects from PDAC (AUC>0.90).

Additionally, LAMC2 was positive in 65% of patients with PDAC who had no CA19.9 elevation. We conclude that LAMC2 is a new serum biomarker for pancreatic adenocarcinoma.

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[189]

TÍTULO / TITLE: - Silencing of GATA6 Suppresses SW1990 Pancreatic Cancer Cell Growth In Vitro and Up-Regulates Reactive Oxygen Species.

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

REVISTA / JOURNAL: - Dig Dis Sci. 2013 Jul 6.

●● Enlace al texto completo (gratuito o de pago) 1007/s10620-013-2752-4

AUTORES / AUTHORS: - Chen WB; Huang FT; Zhuang YY; Tang J; Zhuang XH; Cheng WJ; Gu ZQ; Zhang SN

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, No. 107 Yanjiang West Road, Guangzhou, 510120, Guangdong, People's Republic of China, wenbochen2012@163.com.

RESUMEN / SUMMARY: - BACKGROUND/AIMS: Pancreatic cancer has the worst prognosis of any gastrointestinal cancer with a mortality rate approaching its incidence. Previous studies have indicated that GATA6 plays a key role in organ development and function, and that abnormal expression of GATA6 may induce tumorigenesis. Meanwhile, it has been reported that generation of reactive oxygen species contributes to carcinogenesis. In this study, we set out to study the role of GATA6 expression on proliferation and apoptosis of pancreatic cancer cells and the role of reactive oxygen species. METHODS: Four target miRNA sequences against GATA6 mRNA were synthesized and used to transfect SW1990 cells. Then, GATA6 expression in SW1990 cells was examined by western blot and quantative real-time polymerase chain reaction. Cell proliferation was examined by WST-8 and colony formation assay. Cell cycle progression and apoptosis were measured by flow cytometry. We also measured the generation of reactive oxygen species by immunofluorescence and flow cytometry. RESULTS: RNA interference against GATA6 successfully inhibited mRNA and protein expression of GATA6 in the SW1990 pancreatic cancer cell line. Silencing of GATA6 by RNA interference inhibited cell proliferation and increased apoptosis of SW1990, and enhanced the expression of reactive oxygen species. CONCLUSIONS: These results suggest that the RNA interference approach against GATA6 may be an effective therapeutic approach for treatment of pancreatic cancer.

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[190]

TÍTULO / TITLE: - Cooperation among Numb, MDM2 and p53 in the development and progression of pancreatic cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cell Tissue Res. 2013 Jul 24.
●● Enlace al texto completo (gratuito o de pago) 1007/s00441-013-1679-6
AUTORES / AUTHORS: - Sheng W; Dong M; Zhou J; Li X; Liu Q; Dong Q; Li F
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Gastrointestinal Surgery, The First Hospital, China Medical University, Shenyang, 110001, China.
RESUMEN / SUMMARY: - We study the expression of Numb, MDM2 and p53 for clinical significance in pancreatic cancer (PC) and their functional relationship in regulating biological behaviors of PC cells. IHC, IB and qRT-PCR were used to detect Numb, MDM2 and p53 expression in PC. Transfection and drug intervention were used to investigate their functional relationship in PC cells. IHC showed that Numb expression was negatively associated with tumor size, differentiation and UICC stage, while expression of MDM2 and p53 was positively associated with tumor T and UICC stages, respectively ($P < 0.05$). Numb was an independent prognostic indicator in PC ($P < 0.05$). Patients with Numb-positive expression or combined with MDM2-negative expression had a significantly better overall survival ($P < 0.05$). Altered expression of Numb can regulate wild-type but not mutant p53 expression, while MDM2 knockdown increased Numb but not mutant p53 protein level. Meanwhile, Numb knockdown increased chemoresistance but decreased activated p53 and cleaved-caspase-3 protein expression in gemcitabine-treated Capan-2 cells. Moreover, Numb co-immunoprecipitated with p53 to prevent p53 ubiquitin-dependent protein degradation and this ubiquitin-dependent regulation plays an important role in the coordinate function of these three proteins on cell invasion and migration in PC cells. Our study is the first to demonstrate the clinical significance and functional cooperation among Numb, MDM2 and p53 involved in the development and progression of PC.

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[191]
TÍTULO / TITLE: - Intrahepatic cholangiocarcinoma diagnosed via endoscopic retrograde cholangiopancreatography with a short double-balloon enteroscope.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - World J Gastroenterol. 2013 Jul 21;19(27):4427-31. doi: 10.3748/wjg.v19.i27.4427.
●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i27.4427
AUTORES / AUTHORS: - Ikeura T; Shimatani M; Takaoka M; Matsushita M; Miyoshi H; Kurishima A; Sumimoto K; Miyamoto S; Okazaki K
INSTITUCIÓN / INSTITUTION: - Tsukasa Ikeura, Masaaki Shimatani, Makoto Takaoka, Mitsunobu Matsushita, Hideaki Miyoshi, Akiko Kurishima, Kimi Sumimoto, Sachi Miyamoto, Kazuichi Okazaki, Third Department of Internal Medicine, Kansai Medical University, Osaka 573-1191, Japan.

RESUMEN / SUMMARY: - Endoscopic retrograde cholangiopancreatography (ERCP) using a double-balloon enteroscope (DBE) in patients with bowel reconstruction due to a previous abdominal surgery is now widely accepted. In particular, a short DBE, which has a 2.8-mm working channel and 152-cm working length, is useful for ERCP because of its good rotational and straightening ability and the availability of various conventional ERCP accessories through the working channel. Herein we report a case of intrahepatic cholangiocarcinoma via ERCP with a short DBE. This is the first report in which the pre-cutting and the brush cytological examination were performed successfully under a DBE to diagnose intrahepatic cholangiocarcinoma pathologically. The short DBE allowed us to perform all diagnostic and therapeutic procedures accepted in conventional ERCP in patients with surgically altered anatomies.

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[192]

TÍTULO / TITLE: - Vascular Endothelial Growth Factor Levels in Bile Distinguishes Pancreatic Cancer from Other Etiologies of Biliary Stricture: A Pilot Study.

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

REVISTA / JOURNAL: - Dig Dis Sci. 2013 Jul 5.

●● Enlace al texto completo (gratuito o de pago) 1007/s10620-013-2764-0

AUTORES / AUTHORS: - Navaneethan U; Gutierrez NG; Jegadeesan R; Venkatesh PG; Poptic E; Liu X; Sanaka MR; Jang S; Vargo JJ; Parsi MA

INSTITUCIÓN / INSTITUTION: - Section for Advanced Endoscopy and Pancreatobiliary Disorders, Department of Gastroenterology and Hepatology, Digestive Disease Institute, Desk A30, The Cleveland Clinic, 9500 Euclid Ave., Cleveland, OH, 44195, USA, udhaykumar81@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: Determining the benign or malignant nature of biliary strictures can be challenging. Vascular endothelial growth factor (VEGF) plays an important role in tumor angiogenesis. OBJECTIVE: The purpose of this study was to investigate whether VEGF levels in bile aspirated during endoscopic retrograde cholangiography (ERCP) can distinguish pancreatic cancer from other causes of biliary stricture. METHODS: Bile was directly aspirated in 53 consecutive patients from March 2012 to October 2012 during ERCP from the common bile duct including 15 with pancreatic cancer, 18 with primary sclerosing cholangitis (PSC), nine with cholangiocarcinoma (CCA), and 11 with benign biliary conditions (sphincter of Oddi and choledocholihiasis). Levels of VEGF in bile were measured. The diagnostic performance was then validated in a second, independent validation cohort of 18 patients (pancreatic cancer n = 10, benign n = 8). RESULTS: A total of 53 consecutive patients were recruited. The median bile VEGF levels were significantly elevated in patients with pancreatic cancer (1.9 ng/ml (interquartile

range [IQR] 0.7, 2.2) compared to those with benign biliary conditions (0.3 ng/ml [IQR 0.2, 0.6]; p < 0.001), PSC (0.7 ng/ml [IQR 0.5, 0.9]; p = 0.02) or CCA (0.4 ng/ml [IQR 0.1, 0.5]; p < 0.001). A VEGF cut-off value of 0.5 ng/ml distinguished pancreatic cancer from CCA with a sensitivity and specificity of 93.3 and 88.9 %, respectively, and area under curve (AUC) of 0.93, and from benign conditions with a sensitivity and specificity of 93.3 and 72.7 %, respectively, with AUC of 0.89. The diagnostic accuracy of biliary VEGF was confirmed in the second independent validation cohort. CONCLUSIONS: This study suggests that measurement of biliary VEGF-1 levels distinguishes patients with pancreatic cancer from other etiologies of biliary stricture. This may be particularly relevant in approaching patients with indeterminate biliary stricture.

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[193]

TÍTULO / TITLE: - Nontherapeutic celiotomy incidence is not affected by volume of pancreaticoduodenectomy for pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Am Surg. 2013 Aug;79(8):781-5.

AUTORES / AUTHORS: - Toomey P; Childs C; Luberice K; Ross S; Rosemurgy A

INSTITUCIÓN / INSTITUTION: - The Southeastern Center for Digestive Disorders & Pancreatic Cancer, Advanced Minimally Invasive & Robotic Surgery, Florida Hospital Tampa, Tampa, Florida, USA.

RESUMEN / SUMMARY: - Nontherapeutic celiotomy for pancreatic adenocarcinoma is detrimental to patients by delaying medical treatment as a result of unnecessarily incurred postoperative recovery time. This study was undertaken to evaluate whether surgeon volume of pancreaticoduodenectomy for pancreatic adenocarcinoma impacted the incidence of nontherapeutic celiotomy. All patients undergoing an intended pancreaticoduodenectomy for pancreatic adenocarcinoma were evaluated from 2003 to 2012. Survival was calculated using Kaplan-Meier analysis. The association between surgeon volume of pancreaticoduodenectomy and occurrence of nontherapeutic celiotomy was assessed using Fisher's exact test. Median data are presented. Eight surgeons undertook 443 intended pancreaticoduodenectomies for patients with pancreatic adenocarcinoma; 329 (74%) patients underwent pancreaticoduodenectomy, whereas 114 (26%) patients underwent nontherapeutic celiotomies. Two surgeons undertook 85 per cent of operations. Surgeon volume did not impact the incidence of nontherapeutic celiotomies (P = 0.26). Seventy-seven (68%) patients had metastatic disease at the time of the operation, whereas 37 (32%) patients had locally advanced unresectable disease. These patients had survivals of 5.0 and 6.0 months, respectively (P = 0.77). A high proportion of patients-one in four-undergoing pancreaticoduodenectomy for pancreatic adenocarcinoma will ultimately undergo a nontherapeutic celiotomy. Surgeon volume of pancreaticoduodenectomy for pancreatic adenocarcinoma does not lessen the

incidence of nontherapeutic celiotomies. Preoperative prediction of patients with imaging-occult metastatic or locally advanced disease remains a challenge, even for high-volume surgeons. Attempts to create algorithms for patients with high risk of imaging-occult metastatic or locally advanced disease to undergo staging laparoscopy and/or positron emission tomography scanning may decrease the burden of patients undergoing nontherapeutic celiotomies.

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[194]

TÍTULO / TITLE: - Hemolymphangioma: A rare differential diagnosis of cystic-solid or cystic tumors of the pancreas.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Jun 14;19(22):3520-3. doi: 10.3748/wjg.v19.i22.3520.

●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i22.3520

AUTORES / AUTHORS: - Dong F; Zheng Y; Wu JJ; Fu YB; Jin K; Chao M

INSTITUCIÓN / INSTITUTION: - Fei Dong, Jian-Jun Wu, Kai Jin, Ming Chao, Department of Radiology, the Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310009, Zhejiang Province, China.

RESUMEN / SUMMARY: - We report a case of pancreatic hemolymphangioma. Hemolymphangioma is a malformation of both lymphatic vessels and blood vessels. The incidence of this disease in the pancreas is extremely rare. To the best of our knowledge, only seven cases have been reported worldwide (PubMed). A 39-year-old woman with a one-day history of abdominal pain was admitted to our hospital. There was no obvious precipitating factor. The preoperative examination, including ultrasonography and computed tomography, showed a cystic-solid tumor in the pancreas, and it was considered to be a mucinous cystadenoma or cystadenocarcinoma. Pancreatic body-tail resection combined with splenectomy was performed. After the operation, the tumor was pathologically demonstrated to be a pancreatic hemolymphangioma. Although pancreatic hemolymphangioma is rare, we believe that it should be considered in the differential diagnosis of cystic-solid tumors of the pancreas, particularly when there is no sufficient evidence for diagnosing cystadenoma, cystadenocarcinoma or some other relatively common disease of the pancreas.

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[195]

TÍTULO / TITLE: - The effect of pancreatic juice cytology and/or endoscopic ultrasound-guided fine-needle aspiration biopsy for pancreatic tumor.

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

REVISTA / JOURNAL: - J Gastroenterol Hepatol. 2013 Jul 22. doi: 10.1111/jgh.12332.

●● Enlace al texto completo (gratuito o de pago) 1111/jgh.12332

AUTORES / AUTHORS: - Matsumoto K; Takeda Y; Harada K; Horie Y; Yashima K; Murawaki Y

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Tottori University Hospital, 36-1 Nishi-cho, Yonago 683-8504, Japan.

RESUMEN / SUMMARY: - BACKGROUND/AIM: Endoscopic ultrasound-guided fine needle aspiration biopsy (EUS-FNA) can now provide a cytopathological diagnosis of pancreatic malignancy with higher success rates. However, EUS-FNA cannot be carried out for lesions of minimally invasive carcinoma, because they cannot be detected by endoscopic ultrasonography (EUS), and in cases of intraductal papillary mucinous carcinoma (IPMC), due to the potential for needle tract seeding. A recent study has shown that pancreatic juice cytology (PJC) is useful for diagnosing pancreatic cancer. This study's aim was to evaluate whether PJC strengthens the diagnostic power of EUS-FNA for pancreatic masses. METHODS: A total of 161 patients, who were suspected to have a pancreatic mass on conventional ultrasound and/or computed tomography, was enrolled. RESULTS: EUS-FNA was carried out in 121 cases, and PJC was performed in 83 cases. An adequate specimen was obtained for EUS-FNA in 96.0% and for PJC in 98.9%. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 86.0%, 100%, 100%, 70.5%, and 89.5% for EUS-FNA, and 71.4%, 100%, 100%, 84.4%, and 88.8% for PJC, respectively. EUS-FNA and/or PJC for the diagnosis of pancreatic tumor had a sensitivity of 92.5%, specificity of 100%, positive predictive value of 100%, negative predictive value of 91.7%, and accuracy of 95.9%. The diagnostic accuracy of EUS-FNA and/or PJC was significantly higher than that of EUS-FNA alone or PJC alone. CONCLUSION: PJC improved the diagnostic utility of EUS-FNA for pancreatic tumor.

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[196]

TÍTULO / TITLE: - Upper gastrointestinal complications associated with gemcitabine-concurrent proton radiotherapy for inoperable pancreatic cancer.

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

REVISTA / JOURNAL: - J Gastroenterol. 2013 Jul 12.

●● Enlace al texto completo (gratuito o de pago) 1007/s00535-013-0857-3

AUTORES / AUTHORS: - Takatori K; Terashima K; Yoshida R; Horai A; Satake S; Ose T; Kitajima N; Kinoshita Y; Demizu Y; Fuwa N

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Kasai City Hospital, 1-13 Yokoo, Houjou, Kasai, Hyogo, 675-2393, Japan, kent8t8@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: Little is known about acute upper gastrointestinal (GI) complications associated with gemcitabine-concurrent proton radiotherapy (GPT) for inoperable pancreatic cancer. We investigated acute GI complications following GPT in patients with inoperable pancreatic

cancer using small-bowel endoscopy. METHODS: This prospective single center observational study was conducted at the Hyogo Ion Beam Medical Center from January 2010 to January 2012. Ninety-one patients who had clinically and medically inoperable pancreatic cancer treated by GPT were analyzed. Endoscopic examinations were performed before and after GPT to clarify the incidence rates of radiation-induced ulcers, GI hemorrhage, and GI perforation associated with GPT. RESULTS: Post-treatment endoscopic examinations revealed that 45 (49.4 %) patients had radiation-induced ulcers in the stomach and duodenum. Of those, many ulcerative lesions were found in the lower stomach (51 %) and horizontal part of the duodenum (39 %), regardless of the primary tumor site in the pancreas. Neither GI hemorrhage, nor perforation, was found in post-treatment endoscopy examinations. CONCLUSION: Approximately half of the patients treated with GPT for inoperable pancreatic cancer exhibited radiation-induced ulcers in the stomach and duodenum.

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[197]

TÍTULO / TITLE: - Cystic pancreatic neoplasms: imaging features and management strategy.

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

REVISTA / JOURNAL: - Semin Roentgenol. 2013 Jul;48(3):253-63. doi: 10.1053/j.ro.2013.03.006.

●● Enlace al texto completo (gratuito o de pago) 1053/j.ro.2013.03.006

AUTORES / AUTHORS: - Mortele KJ

INSTITUCIÓN / INSTITUTION: - Harvard Medical School, Boston, MA; Abdominal Imaging and MRI, Beth Israel Deaconess Medical Center, Boston, MA. Electronic address: kmortele@bidmc.harvard.edu.

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[198]

TÍTULO / TITLE: - Staging of pancreatic cancer: role of imaging.

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

REVISTA / JOURNAL: - Semin Roentgenol. 2013 Jul;48(3):245-52. doi: 10.1053/j.ro.2013.03.005.

●● Enlace al texto completo (gratuito o de pago) 1053/j.ro.2013.03.005

AUTORES / AUTHORS: - Al-Hawary MM; Kaza RK; Wasnik AP; Francis IR

INSTITUCIÓN / INSTITUTION: - Diagnostic Radiology, Abdominal Imaging Division, University of Michigan, University Hospital, Ann Arbor, MI. Electronic address: alhawary@med.umich.edu.

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[199]

TÍTULO / TITLE: - Significant efficacy of new transcatheter arterial chemoembolization technique for hepatic metastases of pancreatic neuroendocrine tumors.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Anticancer Res. 2013 Aug;33(8):3355-8.
AUTORES / AUTHORS: - Akahori T; Sho M; Tanaka T; Nishiofuku H; Kinoshita S; Nagai M; Kichikawa K; Nakajima Y
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Nara Medical University, 840 Shijo-cho, Kashihara, Nara, 634-8522, Japan. m-sho@naramed-u.ac.jp.
RESUMEN / SUMMARY: - Background/Aim: The liver is the most frequent site of metastasis of pancreatic neuroendocrine tumors (PNETs). Moreover, hepatic metastasis is a strong prognostic factor for patients with advanced PNETs and is often difficult to treat and cure. PATIENTS AND METHODS: We employed our recently developed new transcatheter arterial chemoembolization technique using a fine-powder formulation of cisplatin mixed with degradable starch microspheres (DSM) for the treatment of unresectable hepatic metastases from PNET in five consecutive patients. RESULTS: A total of 24 sessions of TACE was performed. The responses were complete response in one, partial response in three, and stable disease in one patient. All patients were alive at the time of analysis with a median survival of 36 (3-70) months after the initial treatment of TACE. There were no severe toxicities or adverse effects. CONCLUSION: This new treatment induced a significant effect on hepatic metastases of PNET. The response rate was very high, which has not been achieved even by recent new agents. Our findings may warrant further prospective studies of this therapy.

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[200]
TÍTULO / TITLE: - Hepatobiliary and Pancreatic: A huge liver paraganglioma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Gastroenterol Hepatol. 2013 Jul;28(7):1075. doi: 10.1111/jgh.12254.
●● Enlace al texto completo (gratuito o de pago) 1111/jgh.12254
AUTORES / AUTHORS: - Koh PS; Koong JK; Westerhout CJ; Yoong BK
INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Malaya, Kuala Lumpur.

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[201]
TÍTULO / TITLE: - Hepatobiliary and Pancreatic: Non-cystic intraductal papillary mucinous neoplasm of the pancreas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Gastroenterol Hepatol. 2013 Jul;28(7):1074. doi: 10.1111/jgh.12296.

●● Enlace al texto completo (gratuito o de pago) 1111/jgh.12296

AUTORES / AUTHORS: - Sakamoto K; Hashimoto D; Takamori H; Tokunaga H; Honda Y; Iyama K; Baba H

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery, Kumamoto University, Kumamoto.

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[202]

TÍTULO / TITLE: - Extraskeletal osteosarcoma of the pancreatic head.

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

REVISTA / JOURNAL: - Am Surg. 2013 Aug;79(8):281-3.

AUTORES / AUTHORS: - Resch TR; Hwang SS; Norris CE; Helmer SD; Osborne DL

INSTITUCIÓN / INSTITUTION: - Department of Surgery, The University of Kansas School of Medicine-Wichita, Wichita, Kansas, USA.

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[203]

TÍTULO / TITLE: - The importance of invasion and resection of superior mesenteric and portal veins in adenocarcinoma of the pancreas.

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

REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Jun;60(125):1194-8. doi: 10.5754/hge12171.

●● Enlace al texto completo (gratuito o de pago) 5754/hge12171

AUTORES / AUTHORS: - Aktekin A; Kck M; Odabafi M; Muftuoglu T; Gfcrleyik G; Zkara S; Aker F; Saglam A

RESUMEN / SUMMARY: - Background/Aims: To achieve a negative surgical margin, resection of superior mesenteric/portal vein is necessary in pancreatic cancer. This study is designed to demonstrate the demographic and clinical differences of the patients requiring major vein resection and the incidence of histopathological vein invasion. Methodology: A retrospective analysis of patients that underwent pancreaticoduodenectomy for adenocarcinoma of the pancreas between January 2000 and September 2011 was performed. Macroscopic adhesion to vein was considered as an invasion and a resection was performed. Results: Twenty three of 100 patients that underwent pancreaticoduodenectomy for adenocarcinoma of the pancreas had vein resection. Although the operation time (p=0.001), blood loss (p<0.001) and perioperative blood transfusion (p<0.001) were higher in the vein resection group, there were no differences in perioperative and hospital mortality, complication rate and hospitalization time. The tumor was larger (p=0.001) and lymphovascular invasion (p=0.030), perineural invasion (p=0.011), median metastatic lymph nodes (p=0.007), rate of R1 resection (p=0.007) were higher in vein resection group. Only 9 patients out of 23 patients had histopathological vein wall invasion. Overall survival was also not significantly different (p=0.14).

Conclusions: Overall survival in vein resected group was also not significantly different than patients with standard pancreaticoduodenectomy and not all macroscopic vein adhesion means histopathological vein wall invasion.

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[204]

TÍTULO / TITLE: - Solid pseudo-papillary tumors of the pancreas: current update.

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

REVISTA / JOURNAL: - Abdom Imaging. 2013 Jun 18.

●● Enlace al texto completo (gratuito o de pago) 1007/s00261-013-0015-7

AUTORES / AUTHORS: - Ganeshan DM; Paulson E; Tamm EP; Taggart MW; Balachandran A; Bhosale P

INSTITUCIÓN / INSTITUTION: - Department of Diagnostic Imaging, Body Imaging section, Unit 1473, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX, 77030-4009, USA, dganeshan@mdanderson.org.

RESUMEN / SUMMARY: - Solid pseudo-papillary tumors are rare pancreatic tumors, which occur in females and are typically indolent neoplasms. However, atypical, aggressive variants can occur with locally advanced disease or metastases. They have characteristic imaging features, which vary according to size. This article provides a current update on the molecular biology, histopathology, clinico-radiological features, and management of these tumors.

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[205]

TÍTULO / TITLE: - Comparison of Results between Pylorus-Preserving Pancreaticoduodenectomy and Subtotal Stomach-Preserving Pancreaticoduodenectomy: Report at a Single Cancer Institute.

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

REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Jun;60(125):1182-8. doi: 10.5754/hge11045.

●● Enlace al texto completo (gratuito o de pago) 5754/hge11045

AUTORES / AUTHORS: - Nanashima A; Abo T; Sumida Y; Tobinaga S; Nonaka T; Takeshita H; Hidaka S; Sawai T; Yasutake T; Nagayasu T

RESUMEN / SUMMARY: - Background/Aims: Pylorus-preserving pancreaticoduodenectomy (PPPD) has the advantage of achieving good nutritional status postoperatively, but delayed gastric empty (DGE) is a frequent complication leading to a longer fasting period. Subtotal stomach-preserving pancreaticoduodenectomy (SSPPD) is an alternative option to preserve nutritional status and shorten the fasting period. We retrospectively compared clinical results between PPPD and SSPPD. Methodology: PPPD was performed in 28 patients and SSPPD in 27, between 2000 and 2009. Results: Pancreatic carcinoma was more frequent in the SSPPD group (p = 0.041). Operating time

was longer in the SSPPD group (610 min) than in the PPPD group (540 min; p = 0.031). Blood loss was greater in the SSPPD group (1810 mL) than in the PPPD group (1306 mL; p = 0.048). Period of NG intubation and fasting period were shorter in the SSPPD group (6 days and 9 days, respectively) compared to the PPPD group (15 days and 19 days, respectively; p <0.01 each). Severe DGE was 7% in the SSPPD group and 46% in the PPPD group (p <0.01). Postoperative complications and nutritional status in the early period did not differ between groups, although incidence of fatty liver was higher in the SSPPD group (78%) than in the PPPD group (25%; p <0.01). Conclusions: SSPPD is a useful alternative for pancreaticoduodenectomy. Further prospective studies with longer follow-up are warranted to clarify the superiority and problems associated with this procedure.

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[206]

TÍTULO / TITLE: - Ten cancer associated genes identified in peripheral blood mononuclear cells from patients with pancreatic adenocarcinoma.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Hepatogastroenterology. 2013 Jun 3;60(124):883-9. doi: 10.5754/hge12766.

●● Enlace al texto completo (gratuito o de pago) 5754/hge12766

AUTORES / AUTHORS: - Yan H; Xu L; Jiang W; Xie Q; Dong X; Wu Y
RESUMEN / SUMMARY: - Background/Aims: Identification of biomarkers for pancreatic cancer may help diagnosis and treatment of patients. Methodology: This pilot study evaluated potential markers for pancreatic adenocarcinoma (PAC) in peripheral blood mononuclear cells (PBMC). RNA samples were isolated from PBMCs and hybridized to oligonucleotide arrays. Results: Twenty five-fold leave-two-out analysis identified 10 cancer-associated genes (CAGs). The PAC patients could be identified by the expression profiles of their PBMC with a specificity of 96% and a sensitivity of 80%. Conclusions: Ten CAGs were potential new markers in PBMC for patients with PAC.

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[207]

TÍTULO / TITLE: - Evaluation of radiological prognostic factors of hepatic metastases in patients with non-functional pancreatic neuroendocrine tumors.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Eur J Radiol. 2013 Jul 24. pii: S0720-048X(13)00334-3. doi: 10.1016/j.ejrad.2013.06.017.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ejrad.2013.06.017

AUTORES / AUTHORS: - Denecke T; Baur AD; Ihm C; Steffen IG; Tischer E; Arsenic R; Pascher A; Wiedenmann B; Pavel M

INSTITUCIÓN / INSTITUTION: - Klinik fur Radiologie, Campus Virchow-Klinikum, Charite - Universitatsmedizin Berlin, Germany.

RESUMEN / SUMMARY: - PURPOSE: There are different therapeutic options in non-functional well to moderately differentiated (G1 and G2) pancreatic neuroendocrine tumors (pNET) with unresectable hepatic metastases including systemic chemotherapy and novel molecular targeted therapies. Treatment with somatostatin analogs (SSA) as antiproliferative agents is optional. At initial diagnosis watchful waiting until tumor progression is a well-established approach. Goal of this study was to evaluate imaging features as potential prognostic factors predicting early tumor progression in order to select patients that might benefit from an earlier initiation of medical treatment. PATIENTS AND METHODS: In 44 patients we correlated tumor grade, chromogranin A (CgA) levels, treatment with SSA and imaging features of hepatic metastases on contrast-enhanced multiphase CT and MR imaging with time to tumor progression (TTP) according to RECIST 1.0. RESULTS: In the total patient cohort none of the tested imaging features was found to be a statistically significant prognostic factor for TTP. Since treatment with SSA was associated with an increased TTP we also analyzed a subgroup of 30 patients not treated with SSA. In this subgroup of patients hypoenhancement of hepatic metastases during early contrast phases was found to be a negative prognostic factor for early tumor progression within 12 months (p=0.039). The other evaluated parameters including hepatic tumor load, number of metastases, and presence of regressive morphological changes did not reveal significant results. CONCLUSION: Hypovascularization of liver metastases from G1 and G2 pNET reflected by hypoenhancement during the early contrast phases seems to be associated with early tumor progression. In patients with hypoenhancing metastases repeated biopsy for reassessment of grading of these metastases, and early initiation of therapy should be considered.

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[208]

TÍTULO / TITLE: - Focal autoimmune pancreatitis: Radiological characteristics help to distinguish from pancreatic cancer.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Jun 21;19(23):3634-41. doi: 10.3748/wjg.v19.i23.3634.

●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i23.3634

AUTORES / AUTHORS: - Sun GF; Zuo CJ; Shao CW; Wang JH; Zhang J

INSTITUCIÓN / INSTITUTION: - Gao-Feng Sun, Chang-Jing Zuo, Cheng-Wei Shao, Jian-Hua Wang, Jian Zhang, Department of Radiology, Changhai Hospital, the Second Military Medical University, Shanghai 200433, China.

RESUMEN / SUMMARY: - AIM: To identify the radiological characteristics of focal autoimmune pancreatitis (f-AIP) useful for differentiation from pancreatic cancer (PC). METHODS: Magnetic resonance imaging (MRI) and triple-phase computed tomography (CT) scans of 79 patients (19 with f-AIP, 30 with PC, and 30 with a normal pancreas) were evaluated retrospectively. A radiologist measured the CT attenuation of the pancreatic parenchyma, the f-AIP and PC lesions in triple phases. The mean CT attenuation values of the f-AIP lesions were compared with those of PC, and the mean CT attenuation values of pancreatic parenchyma in the three groups were compared. The diagnostic performance of CT attenuation changes from arterial phase to hepatic phase in the differentiation between f-AIP and PC was evaluated using receiver operating characteristic (ROC) curve analysis. We also investigated the incidence of previously reported radiological findings for differentiation between f-AIP and PC. RESULTS: The mean CT attenuation values of f-AIP lesions in enhanced phases were significantly higher than those of PC (arterial phase: 60 +/- 7 vs 48 +/- 10, P < 0.05; pancreatic phase: 85 +/- 6 vs 63 +/- 15, P < 0.05; hepatic phase: 95 +/- 7 vs 63 +/- 13, P < 0.05). The mean CT attenuation values of f-AIP lesions were significantly lower those of uninvolved pancreas and normal pancreas in the arterial and pancreatic phase of CT (P < 0.001, P < 0.001), with no significant difference at the hepatic phase or unenhanced scanning (P = 0.4, P = 0.1). When the attenuation value increase was equal or more than 28 HU this was considered diagnostic for f-AIP, and a sensitivity of 87.5%, specificity of 100% and an area under the ROC curve of 0.974 (95%CI: 0.928-1.021) were achieved. Five findings were more frequently observed in f-AIP patients: (1) sausage-shaped enlargement; (2) delayed homogeneous enhancement; (3) hypoattenuating capsule-like rim; (4) irregular narrowing of the main pancreatic duct (MPD) and/or stricture of the common bile duct (CBD); and (5) MPD upstream dilation </= 5 mm. CONCLUSION: Analysis of a combination of CT and MRI findings could improve the diagnostic accuracy of differentiating f-AIP from PC.

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[209]

TÍTULO / TITLE: - Synchronous pancreatic solid pseudopapillary neoplasm and intraductal papillary mucinous neoplasm.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Jun 7;19(21):3358-63. doi: 10.3748/wjg.v19.i21.3358.

●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i21.3358

AUTORES / AUTHORS: - Hirabayashi K; Zamboni G; Ito H; Ogawa M; Kawaguchi Y; Yamashita T; Nakagohri T; Nakamura N

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Tokai University School of Medicine, Isehara 259-1193, Japan. khira@is.icc.u-tokai.ac.jp

RESUMEN / SUMMARY: - Solid pseudopapillary neoplasm (SPN) is a rare and low-grade malignant pancreatic neoplasm composed of poorly cohesive monomorphic neoplastic cells forming solid and pseudopapillary structures with frequent hemorrhagic-cystic degeneration. Intraductal papillary mucinous neoplasm (IPMN) is a pancreatic exocrine tumor composed of intraductal papillary growth of mucin containing neoplastic cells in the main pancreatic duct or its major branches. In the case presented here, a 53-year-old, Japanese man was found to have multiple cystic lesions and dilatation of the main pancreatic duct in the neck of the pancreas. Histological examination revealed a main-duct and branch-duct type IPMN, of the gastric-type, involving the neck of the pancreas, associated with a 0.5 cm SPN in the caudal side of the IPMN. We diagnosed this case as synchronous SPN and IPMN. As far as we know, only one other case of synchronous SPN and IPMN has been reported. Both the present case and the previously reported case showed abnormal nuclear expression of beta-catenin in SPN, whereas IPMN showed no abnormal nuclear expression. These results suggest that beta-catenin abnormality is not a common pathogenetic factor of synchronous SPN and IPMN.

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[210]

TÍTULO / TITLE: - Early manifestations of pancreatic cancer: The effect of cancer-nerve interaction.

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

REVISTA / JOURNAL: - Med Hypotheses. 2013 Aug;81(2):180-2. doi: 10.1016/j.mehy.2013.05.010. Epub 2013 Jun 14.

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

1016/j.mehy.2013.05.010

AUTORES / AUTHORS: - Li J; Li Y; Cao G; Guo K; Zhang L; Ma Q

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Second Affiliated Hospital, School of Medicine, Xi'an Jiaotong University, Xi'an, People's Republic of China. Electronic address: ljh991049@yahoo.com.cn.

RESUMEN / SUMMARY: - Clinical manifestation is important for the diagnosis of pancreatic cancer (PanCa). No typical symptoms have been identified that clearly indicate the early stage of PanCa, although most patients with PanCa have symptoms before the cancer is diagnosed. These symptoms are often regarded as common gastrointestinal symptoms and are ignored. The pancreas is richly supplied with nerves, and neuro-cancer interactions begin prior to PanCa cell migration. We hypothesise that the cancer-nerve interaction does generate typical symptoms such as pseudomorphous satiety and mild pain in early PanCa. Constant satiety leads to weight loss. This biological behaviour allows the cancer to progress without attention from the cancer-bearing host. Cancer cells also target the endocrine pancreas, generating a hyperglycaemic state that results in increased energy for cancer cells. The combination of the

so-called common gastrointestinal symptoms and diabetes may represent early typical symptoms of PanCa that can be used to improve early diagnosis.

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[211]

TÍTULO / TITLE: - Management of pancreatic cysts: a multidisciplinary approach.

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

REVISTA / JOURNAL: - Curr Opin Gastroenterol. 2013 Sep;29(5):509-16. doi: 10.1097/MOG.0b013e328363e3b3.

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

1097/MOG.0b013e328363e3b3

AUTORES / AUTHORS: - Law JK; Hruban RH; Lennon AM

INSTITUCIÓN / INSTITUTION: - aDivision of Gastroenterology, Johns Hopkins University School of Medicine bDepartment of Pathology, The Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.

RESUMEN / SUMMARY: - PURPOSE OF REVIEW: An increasing number of patients are being diagnosed with pancreatic cysts. Pancreatic cysts are best evaluated by a team of healthcare professionals that includes gastroenterologists, surgeons, radiologists, pathologists, oncologists and geneticists. RECENT FINDINGS: The international consensus guidelines for the management of intraductal papillary mucinous neoplasm (IPMN) and mucinous cystic neoplasm were updated in 2012, incorporating research that had been reported over a 5-year span since the publication of the previous guidelines. There are significant changes in the new guidelines, which include redefining main duct IPMN and removing the recommendation for surgical resection based on size alone. In addition, the discovery of molecular markers of cyst type promises to revolutionize the way patients are diagnosed and managed. SUMMARY: The diagnosis and management of patients with pancreatic cysts have progressed significantly in recent years. Large prospective, multicenter trials are now needed to validate the new international consensus guidelines and to assess the accuracy of new molecular markers.

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[212]

TÍTULO / TITLE: - Deciphering the role of stroma in pancreatic cancer.

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

REVISTA / JOURNAL: - Curr Opin Gastroenterol. 2013 Sep;29(5):537-43. doi: 10.1097/MOG.0b013e328363affe.

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

1097/MOG.0b013e328363affe

AUTORES / AUTHORS: - Waghray M; Yalamanchili M; Magliano MP; Simeone DM

INSTITUCIÓN / INSTITUTION: - aDepartment of Surgery bDepartment of Cell and Developmental Biology cDepartment of Molecular and Integrative Physiology dTranslational Oncology Program, University of Michigan Medical Center, Ann Arbor, Michigan, USA.

RESUMEN / SUMMARY: - PURPOSE OF REVIEW: This review intends to describe recent studies on pancreatic tumor-associated stroma and potential opportunities and limitations to its targeting. RECENT FINDINGS: One of the defining features of pancreatic cancer is extensive desmoplasia, or an inflammatory, fibrotic reaction. Carcinoma cells live in this complex microenvironment which is comprised of extracellular matrix (ECM), diffusible growth factors, cytokines and a variety of nonepithelial cell types including endothelial cells, immune cells, fibroblasts, myofibroblasts and stellate cells. In addition to the heterogeneity noted in the nonneoplastic cells within the tumor microenvironment, it has also been recognized that neoplastic cancer cells themselves are heterogeneous, and include a subpopulation of stem-cell like cells within tumors termed cancer stem cells. Due to the failure of current therapeutics to improve outcomes in patients with pancreatic cancer, new therapeutic avenues targeting different components of the tumor microenvironment are being investigated. In this review article, we will focus on recent studies regarding the function of the tumor stroma in pancreatic cancer and therapeutic treatments that are being advanced to target the stroma as a critical part of tumor management. SUMMARY: Recent studies have shed new light on the contribution of the pancreatic cancer fibroinflammatory stroma to pancreatic cancer biology. Additional studies are needed to better define its full contribution to tumor behavior and how to best understand the optimal ways to develop therapies that counteract its pro-neoplastic properties.

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[213]

TÍTULO / TITLE: - Disease-specific mortality among patients with intraductal papillary mucinous neoplasm of the pancreas.

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

REVISTA / JOURNAL: - Clin Gastroenterol Hepatol. 2013 Jul 24. pii: S1542-3565(13)01054-9. doi: 10.1016/j.cgh.2013.06.032.

●● Enlace al texto completo (gratuito o de pago) 1016/j.cgh.2013.06.032

AUTORES / AUTHORS: - Kawakubo K; Tada M; Isayama H; Sasahira N; Nakai Y; Takahara N; Uchino R; Hamada T; Miyabayashi K; Yamamoto K; Mizuno S; Mohri D; Kogure H; Sasaki T; Yamamoto N; Hirano K; Ijichi H; Tateishi K; Koike K

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Intraductal papillary mucinous neoplasm (IPMN) of the pancreas is associated with synchronous and metachronous pancreatic cancer. However, the risk factors for pancreatic

cancer-specific mortality have not been determined. We evaluated disease-specific mortality among patients with IPMNs harboring high-risk stigmata. METHODS: We analyzed data from 243 patients diagnosed with IPMN, with indications for surgery according to the consensus criteria, at the University of Tokyo Hospital from 1995 to January 2011. Using optimal matching and propensity scores based on 16 characteristics, we matched patients who underwent surgery at diagnosis with those who did not undergo surgery. Fine and Gray competing risk analysis was used to assess the risk of pancreatic cancer-specific mortality. RESULTS: Fifty-nine patients underwent surgery following diagnosis and 184 did not. After adjustment with propensity scores, detection of a hypo-attenuating area by computed tomography, which indicates invasive carcinoma, was significantly associated with pancreatic cancer-specific mortality (adjusted hazard ratio, 16.75; 95% confidence interval, 2.72-103.3; P=.002). Cyst diameter, main pancreatic duct diameter, and the presence of a mural nodule were not significantly associated with pancreatic cancer-specific mortality. Surgical management was found to reduce pancreatic cancer-specific mortality, especially in patients with hypo-attenuating areas (P=.038). CONCLUSIONS: Detection of a hypo-attenuating area by computed tomography significantly increases risk for pancreatic cancer-specific mortality among IPMN patients with consensus indications for surgery. Surgical resection significantly reduces this risk.

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[214]

TÍTULO / TITLE: - Rapid deaminator status is associated with poor clinical outcome in pancreatic cancer patients treated with a gemcitabine-based regimen.

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

REVISTA / JOURNAL: - Pharmacogenomics. 2013 Jul;14(9):1047-51. doi: 10.2217/pgs.13.93.

●● Enlace al texto completo (gratuito o de pago) 2217/pgs.13.93

AUTORES / AUTHORS: - Serdjebi C; Seitz JF; Ciccolini J; Duluc M; Norguet E; Fina F; Lacarelle B; Ouafik L; Dahan L

INSTITUCIÓN / INSTITUTION: - Transfer Oncology Laboratory, Nord University Hospital of Marseille, Inserm S_911 CRO2, Aix-Marseille University, Marseille, France.

RESUMEN / SUMMARY: - Background: Gemcitabine is a mainstay in the treatment of biliary and pancreatic cancers, with limited efficacy in most settings. The gemcitabine elimination pattern is primarily driven by deamination in the liver by CDA. CDA is affected by genetic polymorphisms, leading to marked variations in activity and, subsequently, to erratic drug plasma exposures in patients administered with standard dosage. CDA deficiency has been a rising concern with gemcitabine since several studies have proven that poor metabolizer patients experience life-threatening toxicities upon drug intake.

In theory, ultrarapid metabolizer (UM) patients should be conversely at risk of treatment failure, although thus far few studies have addressed this issue in digestive oncology. Patients & methods: A pilot study was conducted on 40 pancreatic cancer patients, all treated with gemcitabine-based therapy. CDA status was primarily established on a phenotypic basis determined by measurement of residual CDA enzymatic activity in serum. Additionally, a search for c208G>A and c79A>C polymorphisms was carried out. Results: No patients carrying c208G>A polymorphisms were found, and only heterozygous c79A>C patients were observed. Eight out of the 40 patients (i.e., 20%) were identified as UM, with CDA activities over 6 U/mg. CDA activity was significantly different between progressive disease patients and patients with controlled disease (8.4 vs 3 U/mg; $p < 0.001$). Conversely, fewer gemcitabine-related severe toxicities were observed in UM patients. Conclusion: This pilot study strongly suggests that UM patients are nearly five-times more likely to have progressive disease than patients with normal or low CDA activities, and that beside molecular events at the tumor level, upstream deregulations affecting drug disposition should be taken into account. Original submitted 12 March 2013; Revision submitted 3 May 2013.

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[215]

- CASTELLANO -

TÍTULO / TITLE: Therapieerfolg nach neoadjuvanter Radiochemotherapie und Korrelation mit dem Ernahrungsstatus bei Patienten mit lokal fortgeschrittenem Pankreaskarzinom.

TÍTULO / TITLE: - Outcome after neoadjuvant chemoradiation and correlation with nutritional status in patients with locally advanced pancreatic cancer.

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

REVISTA / JOURNAL: - Strahlenther Onkol. 2013 Jul 31.

●● Enlace al texto completo (gratuito o de pago) 1007/s00066-013-0393-3

AUTORES / AUTHORS: - Naumann P; Habermehl D; Welzel T; Debus J; Combs SE

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University Clinic Heidelberg, Im Neuenheimer Feld 400, 69120, Heidelberg, Germany, Patrick.Naumann@med.uni-heidelberg.de.

RESUMEN / SUMMARY: - BACKGROUND: Cancer patients commonly suffer from weight loss since rapid tumor growth can cause catabolic metabolism and depletion of energy stores such as abdominal fat. In locally advanced pancreatic cancer this is even more pronounced due to abdominal pain, fatigue, nausea or malnutrition. In the present article, we quantify this frequently observed weight loss and assess its impact on outcome and survival. METHODS: Data on demographics, biometrics, toxicity and survival were

collected for the last 100 patients treated with neoadjuvant chemoradiation for locally advanced pancreatic cancer at our department (45.0 Gy and boost up to 54.0 Gy plus concurrent and subsequent gemcitabine), and the subcutaneous fat area at the umbilicus level was measured by computer tomography before and after chemoradiation. RESULTS: After chemoradiation, patients showed a highly statistically significant weight loss and reduction of the subcutaneous fat area. We could determine a very strong correlation of subcutaneous fat area to patient BMI. By categorizing patients according to their BMI based on the WHO classification as slender, normal, overweight and obese, we found improved but not statistically significant survival among obese patients. Accordingly, patients who showed less weight loss tended to survive longer. CONCLUSIONS: In this study, patients with pancreatic cancer lost weight during chemoradiation and their subcutaneous fat diminished. Changes in subcutaneous fat area were highly correlated with patients' BMI. Moreover, obese patients and patients who lost less weight had an improved outcome after treatment. Although the extent of weight loss was not significantly correlated with survival, the observed trend warrants greater attention to nutritional status in the future.

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[216]

TÍTULO / TITLE: - Pancreatic enzyme replacement therapy for enterally fed patients with cystic fibrosis.

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

REVISTA / JOURNAL: - Nutr Clin Pract. 2013 Aug;28(4):485-9. doi: 10.1177/0884533613491786. Epub 2013 Jun 10.

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

1177/0884533613491786

AUTORES / AUTHORS: - Nicolo M; Stratton KW; Rooney W; Boullata J

INSTITUCIÓN / INSTITUTION: - Joseph Boullata, RPh, University of Pennsylvania, 418 Curie Blvd, Philadelphia, PA 19104, USA. Email: boullata@nursing.upenn.edu.

RESUMEN / SUMMARY: - Administration of pancreatic enzymes (pancrelipase) to adult patients with cystic fibrosis when receiving enteral nutrition through a feeding tube is challenging. A number of techniques for preparing and administering the drug may result in complications that include feeding tube occlusion and inadequate enzyme delivery to the patient. A series of inpatient encounters is described.

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[217]

TÍTULO / TITLE: - Splenic Vein Thrombosis Is Associated with an Increase in Pancreas-Specific Complications and Reduced Survival in Patients Undergoing Distal Pancreatectomy for Pancreatic Exocrine Cancer.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Jun 25.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2260-z

AUTORES / AUTHORS: - Dedania N; Agrawal N; Winter JM; Koniaris LG; Rosato EL; Sauter PK; Leiby B; Pequignot E; Yeo CJ; Lavu H

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Thomas Jefferson University, Jefferson Pancreas, Biliary and Related Cancer Center, 1025 Walnut Street, College Bldg., Suite 605, Philadelphia, PA, 19107, USA.

RESUMEN / SUMMARY: - Distal pancreatectomy and splenectomy (DPS) is the procedure of choice for the surgical treatment of pancreatic exocrine cancer localized to the body and tail of the pancreas. Splenic vein thrombosis (SVT) can occur in patients with malignant pancreatic exocrine tumors secondary to direct tumor invasion or compression of the splenic vein by mass effect. This study examines the effect of preoperative SVT on postoperative outcomes. In this retrospective cohort study, we queried our pancreatic surgery database to identify patients who underwent DPS from October 2005 to June 2011. These cases were evaluated for evidence of preoperative SVT on clinical records and cross-sectional imaging (CT, MRI, endoscopic US). Outcomes for patients with and without SVT were compared. From an overall cohort of 285 consecutive patients who underwent DPS during the study period, data were evaluated for 70 subjects who underwent surgery for pancreatic exocrine cancer (27 with SVT, 43 without SVT). The preoperative demographics and co-morbidities were similar between the groups, except the average age was higher for those without SVT ($p < 0.05$). The median estimated blood loss was significantly higher in the SVT group (675 versus 250 ml, $p = <0.001$). While the overall morbidity rates were similar between the two groups (48 % SVT versus 56 % no SVT, p = NS), the group with SVT had a significantly higher rate of pancreas-specific complications, including pancreatic fistula (33 versus 7 %, $p < 0.01$) and delayed gastric emptying (15 versus 0 %, $p < 0.02$). Hospital readmission rates were similar between the groups (30 versus 28 %, p = NS). Patients without SVT had a trend toward longer median survival (40 versus 20.8 months), although the difference was not statistically significant ($p = 0.1$). DPS for pancreatic ductal adenocarcinoma can be performed safely in patients with SVT, but with higher intraoperative blood loss, increased pancreas-specific complications, and a trend towards lower long-term survival rates. This paper was presented as a poster at the 53rd annual meeting of the Society for Surgery of the Alimentary Tract and at the 46th annual meeting of the Pancreas Club, San Diego, CA, May 2012.

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[218]

TÍTULO / TITLE: - An evaluation of neoadjuvant chemoradiotherapy for patients with resectable pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - HPB Surg. 2013;2013:298726. doi: 10.1155/2013/298726. Epub 2013 Jun 20.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/298726

AUTORES / AUTHORS: - Jiang H; Du C; Cai M; He H; Chen C; Qiu J; Wu H

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Pancreatic Surgery, The Second People's Hospital of Neijiang, Luzhou Medical College, Neijiang, Sichuan 641003, China.

RESUMEN / SUMMARY: - Aims. The aim of this study is to compare our results of preoperative chemotherapy followed by pancreaticoduodenectomy (PD) with those of surgery alone in patients with localized resectable pancreatic ductal adenocarcinoma (PDAC). Methods. Outcome data for 112 patients of resectable PDAC who received preoperative chemoradiotherapy followed by PD (group I) between January 2004 and April 2010 were retrospectively analyzed and were compared with selected 120 patients who underwent PD alone (group II) in the same period. Results. Patients in group I had an incidence of locoregional recurrence of 17.1% compared to 30.8% in group II (P = 0.03). There were no statistically significant differences in postoperative morbidity (27.7% versus 30.8%) and mortality (2.67% versus 3.33%). The 1-, 2-, and 3-year survival rates were estimated at 82.1%, 54%, and 28%, respectively, with NCRT and 65.8%, 29.1%, and 10% without (P = 0.006). Nevertheless, preoperative chemotherapy did not reduce the 1-, 3-, and 5-year disease-free survival rates, which were estimated at 58%, 36.6%, and 12.5% with NCRT and 51.7%, 18.3%, and 7.5% without (P = 0.058). Conclusions. The treatment of NCRT followed by PD in patients with PDAC has a significantly lower rate of locoregional recurrence and a longer overall survival than those with surgery alone.

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[219]

TÍTULO / TITLE: - Role of adipocytokines and its correlation with endocrine pancreatic function in patients with pancreatic cancer.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Jul-Aug;13(4):409-14. doi: 10.1016/j.pan.2013.04.198. Epub 2013 May 9.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.04.198

AUTORES / AUTHORS: - Gasiorowska A; Talar-Wojnarowska R; Kaczka A; Borkowska A; Czupryniak L; Malecka-Panas E

INSTITUCIÓN / INSTITUTION: - Department of Digestive Tract Diseases, Medical University of Lodz, Kopcinskiego 22, 90-153 Lodz, Poland. Electronic address: anita@sofcom.pl.

RESUMEN / SUMMARY: - INTRODUCTION: Some authors suggest that adipocytokines contribute to the induction of pancreatic carcinogenesis as well as the development of endocrine insufficiency. AIMS: We evaluate the circulating concentrations of leptin, resistin and visfatin in patients with newly

diagnosed pancreatic cancer (PC) and relationship between serum adipocytokines level and clinicopathological features of PC. Moreover the usefulness of those adipocytokines as possible biomarkers of endocrine pancreatic function in PC has been assessed. METHODS: The pilot study group consisted of 45 individuals (mean age 65.6 +/- 11.5 years, BMI 21.8 +/- 3.4 kg/m(2)) with newly diagnosed PC (within last 1-3 months) and 13 healthy individuals with age, gender and BMI matched to the study group. Among PC patients 18 (40%) had recently diagnosed diabetes. Fasting plasma leptin, resistin, visfatin concentrations were determined with ELISA (R&D Systems, Phoenix Pharmaceuticals) and insulin by RIA (DakoCytomation). RESULTS: Patients with PC as compared to controls had significantly lower plasma leptin (40.6 +/- 21.3 vs 63.2 +/- 16.3 pg/mL; p < 0,0008). In contrast PC patients showed more than six fold higher level of resistin (126.2 +/- 143.2 vs 18.9 +/- 7.2 ng/mL; p < 0.009) than controls. The median plasma visfatin was 2.8 +/- 1.8 ng/mL, which was not significantly different from the controls (3.8 +/- 1.1 ng/mL). When PC patients with and without diabetes were considered separately, plasma leptin concentrations among nondiabetic patients were slightly, but not significantly higher (44.6 +/- 21.0) as compared to diabetics (34.5 +/- 20.7). Moreover there was no difference between visfatin and resistin level in PC, among patients with and without diabetes. No significant differences between serum level of leptin, visfatin and resistin and age, gender, BMI, smoking status, tumor localization, distant metastases and pain has been found. CONCLUSION: The results of this study confirm previous findings that patients with newly diagnosed pancreatic cancer are characterized with lower level of leptin. This pilot study showed significantly higher resistin concentrations in patients with PC in comparison to healthy controls, which may be helpful in PC early diagnosis. Changes in leptin and resistin level in PC are not likely related to endocrine disorders.

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[220]

TÍTULO / TITLE: - Intraductal papillary mucinous neoplasm of the pancreas and IgG4-related disease: A coincidental association.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Jul-Aug;13(4):379-83. doi: 10.1016/j.pan.2013.04.197. Epub 2013 Apr 26.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.04.197

AUTORES / AUTHORS: - Tabata T; Kamisawa T; Hara S; Kuruma S; Chiba K; Kuwata G; Fujiwara T; Egashira H; Koizumi S; Endo Y; Koizumi K; Fujiwara J; Arakawa T; Momma K; Horiguchi S; Hishima T; Kurata M; Honda G; Kloppel G

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Tokyo Metropolitan Komagome Hospital, 3-18-22 Honkomagome, Bunkyo-ku, Tokyo 113-8677, Japan.

RESUMEN / SUMMARY: - BACKGROUND/AIMS: Coexistence of autoimmune pancreatitis (AIP) and pancreatic cancer, elevation of serum IgG4 levels in pancreatic cancer patients, and infiltration of IgG4-positive plasma cells in peritumorous pancreatitis have been described in a few reports. This study examined the relationship between intraductal papillary mucinous neoplasm (IPMN) of the pancreas and peritumorous IgG4-positive lymphoplasmacytic infiltrates. METHODS: Serum IgG4 levels were measured in 54 patients with IPMN (median 70 years, 26 males and 28 females; 13 main duct type and 41 branch duct type). Histological findings focusing on dense lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis were reviewed, and immunostaining with IgG4 and IgG was performed in 23 surgically resected IPMN cases (18 main duct type and 5 branch duct type). The presence of IgG4-positive plasma cells >10/hpf and an IgG4-positive/IgG-positive plasma cell ratio >40% were considered significant. RESULTS: Serum IgG4 levels were elevated in 2 (4%) IPMN patients. Significant infiltration of IgG4-positive plasma cells was detected in 4 IPMN cases (17%). The IgG4-positive/IgG-positive plasma cell ratio was >40% in all 4 cases. In one case with a markedly elevated serum IgG4 level (624 mg/dL), typical lymphoplasmacytic sclerosing pancreatitis (AIP type 1) lesions surrounded the whole IPMN. In the 3 other cases, infiltration of IgG4-positive plasma cells with fibrosis was focally detected mainly in the periductal area around the IPMN. CONCLUSIONS: In a few patients with IPMNs, IgG4-positive plasma cell infiltration can occur in the peritumorous area. The association of an IPMN with AIP type 1-like changes seems to be exceptional and coincidental.

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[221]

TÍTULO / TITLE: - Experimental studies on treatment of pancreatic cancer with double-regulated duplicative adenovirus AdTPHre-hEndo carrying human endostatin gene.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Jul-Aug;13(4):393-400. doi: 10.1016/j.pan.2013.05.012. Epub 2013 Jun 14.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.05.012

AUTORES / AUTHORS: - Shan YF; Fang YF; Wang XQ; Jin R; Zhang QY; Andersson R

INSTITUCIÓN / INSTITUTION: - Department of Surgery, First Affiliated Hospital, Wenzhou Medical College, Wenzhou 325000, Zhejiang Province, China.

RESUMEN / SUMMARY: - BACKGROUND: Gene-virus targeted therapy is a promising new method of treating pancreatic cancer. To increase the efficacy and decrease the side-effect, we constructed a conditionally replicative adenovirus (CRAd) expressing human endostatin, with a human Telomoerase Reverse Transcriptase (hTERT) promoter for the regulation of the early stage of adenovirus expression of gene E1a and a Hypoxia Response Element (HRE)

promoter to regulate the gene E1b. METHODS: A gene recombination technique was adopted to construct and generate the adenovirus AdTPHre-hEndo. Pancreatic cancer cells were studied both in vitro and in vivo. Western blotting was adopted to observe the expressions of protein E1A and E1B; duplication assay was applied to observe the selective duplication capability of recombinant cells. MTT assay was applied to measure the lethal effects of virus on pancreatic cancer cells, and ELISA was adopted to detect the human endostatin gene expression. A pancreatic cancer transplantation tumor model of nude mice was constructed to observe the antitumor effects of the virus. RESULTS: Double-regulated duplicative adenovirus AdTPHre-hEndo genes were successfully constructed. Duplication and lethal assays proved that AdTPHre-hEndo could replicate specifically in pancreatic cancer cells and kill them. The endostatin expression in a cultured supernatant from tumor cells was significantly higher than that obtained from non-duplicative adenovirus vectors carrying that gene. The animal experiment demonstrated that AdTPHre-hEndo has a high capability to limit pancreatic cancer growth. CONCLUSIONS: AdTPHre-hEndo has a special ability to duplicate and kill pancreatic cancer cells in in vitro and in vivo experiments, thus providing a new gene-virus-based treatment system for pancreatic cancer.

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[222]

TÍTULO / TITLE: - Intake of Coffee, Decaffeinated Coffee, or Tea Does Not Affect Risk for Pancreatic Cancer: Results From the European Prospective Investigation into Nutrition and Cancer Study.

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

REVISTA / JOURNAL: - Clin Gastroenterol Hepatol. 2013 Jun 10. pii: S1542-3565(13)00774-X. doi: 10.1016/j.cgh.2013.05.029.

●● Enlace al texto completo (gratuito o de pago) 1016/j.cgh.2013.05.029

AUTORES / AUTHORS: - Bhoo-Pathy N; Uiterwaal CS; Dik VK; Jeurnink SM; Bech BH; Overvad K; Halkjaer J; Tjonneland A; Boutron-Ruault MC; Fagherazzi G; Racine A; Katzke VA; Li K; Boeing H; Floegel A; Androulidaki A; Bamia C; Trichopoulou A; Masala G; Panico S; Crosignani P; Tumino R; Vineis P; Peeters PH; Gavrilyuk O; Skeie G; Weiderpass E; Duell EJ; Arguelles M; Molina-Montes E; Navarro C; Ardanaz E; Dorronsoro M; Lindkvist B; Wallstrom P; Sund M; Ye W; Khaw KT; Wareham N; Key TJ; Travis RC; Duarte-Salles T; Freisling H; Licaj I; Gallo V; Michaud DS; Riboli E; Bueno-de-Mesquita HB

INSTITUCIÓN / INSTITUTION: - Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands; Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; National Clinical Research Centre, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia.

RESUMEN / SUMMARY: - BACKGROUND & AIMS: Few modifiable risk factors have been implicated in the etiology of pancreatic cancer. There is little

evidence for the effects of caffeinated coffee, decaffeinated coffee, or tea intake on risk of pancreatic cancer. We investigated the association of total coffee, caffeinated coffee, decaffeinated coffee, and tea consumption with risk of pancreatic cancer. METHODS: This study was conducted within the European Prospective Investigation into Nutrition and Cancer cohort, comprising male and female participants from 10 European countries. Between 1992 and 2000, there were 477,312 participants without cancer who completed a dietary questionnaire, and were followed up to determine pancreatic cancer incidence. Coffee and tea intake was calibrated with a 24-hour dietary recall. Adjusted hazard ratios (HRs) were computed using multivariable Cox regression. RESULTS: During a mean follow-up period of 11.6 y, 865 first incidences of pancreatic cancers were reported. When divided into fourths, neither total intake of coffee (HR, 1.03; 95% confidence interval [CI], 0.83-1.27; high vs low intake), decaffeinated coffee (HR, 1.12; 95% CI, 0.76-1.63; high vs low intake), nor tea were associated with risk of pancreatic cancer (HR, 1.22, 95% CI, 0.95-1.56; high vs low intake). Moderately low intake of caffeinated coffee was associated with an increased risk of pancreatic cancer (HR, 1.33; 95% CI, 1.02-1.74), compared with low intake. However, no graded dose response was observed, and the association attenuated after restriction to histologically confirmed pancreatic cancers. CONCLUSIONS: Based on an analysis of data from the European Prospective Investigation into Nutrition and Cancer cohort, total coffee, decaffeinated coffee, and tea consumption are not related to the risk of pancreatic cancer.

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[223]

TÍTULO / TITLE: - Caution in interpretation of the tumor marker CA 19.9 in patients with obstructive jaundice: illustrative case reports.

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

REVISTA / JOURNAL: - J Miss State Med Assoc. 2013 Apr;54(4):96-9.

AUTORES / AUTHORS: - Helling TS

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University of Mississippi Medical Center, 2500 North State Street, Jackson, MS 39216, USA. thelling@umc.edu

RESUMEN / SUMMARY: - BACKGROUND: Carbohydrate antigen (CA) 19.9 is a Lewis blood group oligosaccharide antigen which exists in fixed and soluble forms. The CA 19.9 antigen is synthesized by epithelial cells of the gastrointestinal tract, pancreatic duct, and biliary tree. The CA 19.9 antigen is commonly used as a tumor marker for malignancies of the pancreas and biliary tract. High levels (> 300 U/ml) of antigen have strongly suggested malignant processes. METHODS: Four patients are described with markedly elevated levels of CA 19.9 due to benign calculous disease. RESULTS: Three of four patients underwent endoscopic stone removal followed by cholecystectomy; the fourth patient spontaneously passed stones and had a subsequent

cholecystectomy with benign inflammatory pathology. Removal or passage of the obstructing stones produced normalization of the CA 19.9 in each case even with long-term follow-up up to one year. All pathology specimens were interpreted as benign. CONCLUSIONS: Marked elevations of CA 19.9 may be found in benign obstructive disease and should be interpreted with caution until biliary obstruction is relieved.

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[224]

TÍTULO / TITLE: - Circulating peripheral blood mononuclear cells exhibit altered miRNA expression patterns in pancreatic cancer.

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

REVISTA / JOURNAL: - Expert Rev Mol Diagn. 2013 Jun;13(5):425-30. doi: 10.1586/erm.13.31.

●● Enlace al texto completo (gratuito o de pago) 1586/erm.13.31

AUTORES / AUTHORS: - Frampton AE; Fletcher CE; Gall TM; Castellano L; Bevan CL; Stebbing J; Krell J

INSTITUCIÓN / INSTITUTION: - HPB Surgical Unit, Department of Surgery & Cancer, Imperial College, Hammersmith Hospital Campus, Du Cane Road, London, W12 0HS, UK. a.frampton@imperial.ac.uk.

RESUMEN / SUMMARY: - Evaluation of: Wang WS, Liu LX, Li GP et al. Combined serum CA19-9 and miR-27ª-3p in peripheral blood mononuclear cells to diagnose pancreatic cancer. Cancer Prev. Res. (Phila.) 6(4), 331-338 (2013). Patients with pancreatic ductal adenocarcinoma (PDAC) have a bleak outlook, primarily because tumors are detected late and are often too advanced for surgical resection. In addition, these lesions are incredibly resistant to anticancer therapies. The majority of PDAC patients have impaired tumor immunity, contributing to disease development and progression, although the mechanisms remain poorly understood. miRNAs are important negative gene regulators that have critical roles in human tumorigenesis. Blood-based miRNAs have been investigated as biomarkers for various cancers, in the hope that these will outperform current serum tumor markers. The evaluated study examined the miRNA profiles in peripheral blood mononuclear cells from PDAC patients. The theory is that circulating blood cells monitor the patients' physiological state and respond by altering their transcriptome and that this can then be used to detect disease. In this article, we have examined the evidence for using circulating miRNAs to diagnose/prognose PDAC.

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[225]

TÍTULO / TITLE: - Genistein Down-Regulates miR-223 Expression in Pancreatic Cancer Cells.

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

REVISTA / JOURNAL: - Curr Drug Targets. 2013 Sep;14(10):1150-6.

AUTORES / AUTHORS: - Ma J; Cheng L; Liu H; Zhang J; Shi Y; Zeng F; Miele L; Sarkar FH; Xia J; Wang Z

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Bengbu Medical College, Anhui, 233030, China. zhiwei@gmail.com.

RESUMEN / SUMMARY: - Although genistein has been shown to inhibit tumorigenesis in a variety of human cancers including pancreatic cancer (PC), the exact molecular mechanism of its anti-cancer effects has not yet been fully elucidated. Recently, microRNAs (miRNAs) have been reported to regulate multiple aspects of tumor development and progression, indicating that targeting miRNAs could be a novel strategy to treat human cancers. In the current study, we investigated whether a natural compound genistein could down-regulate onco-miR-223, resulting in the inhibition of cell growth and invasion, and induction of apoptosis in PC cells. We found that genistein treatment significantly inhibited miR-223 expression and up-regulated Fbw7, one of the targets of miR-223. Moreover, down-regulation of miR-223 inhibited cell growth and induced apoptosis in PC cells. These findings suggest that genistein exerts its anti-tumor activity partly through downregulation of miR-223 in PC cells.

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[226]

TÍTULO / TITLE: - Apoptosis of Human Pancreatic Carcinoma PC-2 Cells by an Antisense Oligonucleotide Specific to Point Mutated K-ras.

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

REVISTA / JOURNAL: - Pathol Oncol Res. 2013 Jul 5.

●● Enlace al texto completo (gratuito o de pago) 1007/s12253-013-9661-x

AUTORES / AUTHORS: - Yongxiang W; Liang G; Qinshu S

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Zhejiang Provincial People's Hospital, Hangzhou, 310014, China.

RESUMEN / SUMMARY: - The prognosis of pancreatic carcinoma is poor due to the difficulty in early diagnosis, insensitivity to routine therapies and limited understanding of its pathological mechanisms. Gene therapy is now becoming an important strategy for the treatment of pancreatic carcinoma, which includes antisense gene therapy. In this study, we investigated the effect of an antisense oligonucleotide specific to point mutated K-ras on the apoptosis of human pancreatic carcinoma cells in vitro. Human pancreatic carcinoma PC-2 cells were transfected with an antisense oligonucleotide specific to a K-ras point mutation by liposomes. The effect of the antisense oligonucleotide on the apoptosis of PC-2 cells was studied using flow cytometry, TUNEL, and phase contrast microscopy. An apoptotic peak was observed in the experimental group, and most cells were arrested at the G1 phase with few cells at the S phase. The numbers of apoptotic cells in the experimental group increased as indicated by TUNEL and phase contrast microscopy. An antisense

oligonucleotide specific to a K-ras point mutation promotes apoptosis in PC-2 cells in vitro perhaps by inhibition of ras gene expression.

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[227]

TÍTULO / TITLE: - Inhibition of oncogenic Pim-3 kinase modulates transformed growth and chemosensitizes pancreatic cancer cells to gemcitabine.

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

REVISTA / JOURNAL: - Cancer Biol Ther. 2013 Jun;14(6):492-501. doi: 10.4161/cbt.24343.

●● Enlace al texto completo (gratuito o de pago) 4161/cbt.24343

AUTORES / AUTHORS: - Xu D; Cobb MG; Gavilano L; Witherspoon SM; Williams D; White CD; Taverna P; Bednarski BK; Kim HJ; Baldwin AS; Baines AT

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Marine Environmental Science, Xiamen University, Xiamen, China.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) is a lethal cancer with a 5-year survival rate of only 6%. Although the cytosine analog gemcitabine is the drug commonly used to treat PDAC, chemoresistance unfortunately renders the drug ineffective. Thus, strategies that can decrease this resistance will be essential for improving the dismal outcome of patients suffering from this disease. We previously observed that oncogenic Pim-1 kinase was aberrantly expressed in PDAC tissues and cell lines and was responsible for radioresistance. Furthermore, members of the Pim family have been shown to reduce the efficacy of chemotherapeutic drugs in cancer. Therefore, we attempted to evaluate the role of Pim-3 in chemoresistance of PDAC cells. We were able to confirm upregulation of the Pim-3 oncogene in PDAC tissues and cell lines versus normal samples. Biological consequences of inhibiting Pim-3 expression with shRNA-mediated suppression included decreases in anchorage-dependent growth, invasion through Matrigel and chemoresistance to gemcitabine as measured by caspase-3 activity. Additionally, we were able to demonstrate that Pim-1 and Pim-3 play overlapping but non-identical roles as it relates to gemcitabine sensitivity of pancreatic cancer cells. To further support the role of Pim-3 suppression in sensitizing PDAC cells to gemcitabine, we used the pharmacological Pim kinase inhibitor SGI-1776. Treatment of PDAC cells with SGI-1776 resulted in decreased phosphorylation of the proapoptotic protein Bad and cell cycle changes. When SGI-1776 was combined with gemcitabine, there was a greater decrease in cell viability in the PDAC cells versus cells treated with either of the drugs separately. These results suggest combining drug therapies that inhibit Pim kinases, such as Pim-3, with chemotherapeutic agents, to aid in decreasing chemoresistance in pancreatic cancer.

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[228]

TÍTULO / TITLE: - Inhibition of checkpoint kinase 2 (CHK2) enhances sensitivity of pancreatic adenocarcinoma cells to gemcitabine.

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

REVISTA / JOURNAL: - J Cell Mol Med. 2013 Jul 16. doi: 10.1111/jcmm.12101.

●● Enlace al texto completo (gratuito o de pago) 1111/jcmm.12101

AUTORES / AUTHORS: - Duong HQ; Hong YB; Kim JS; Lee HS; Yi YW; Kim YJ; Wang A; Zhao W; Cho CH; Seong YS; Bae I

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; WCU (World Class University) Research Center of Nanobiomedical Science, Dankook University, Cheonan, Korea.

RESUMEN / SUMMARY: - Checkpoint kinase 2 (CHK2) plays pivotal function as an effector of cell cycle checkpoint arrest following DNA damage. Recently, we found that co-treatment of NSC109555 (a potent and selective CHK2 inhibitor) potentiated the cytotoxic effect of gemcitabine (GEM) in pancreatic cancer MIA PaCa-2 cells. Here, we further examined whether NSC109555 could enhance the antitumour effect of GEM in pancreatic adenocarcinoma cell lines. In this study, the combination treatment of NSC109555 plus GEM demonstrated strong synergistic antitumour effect in four pancreatic cancer cells (MIA PaCa-2, CFPAC-1, Panc-1 and BxPC-3). In addition, the GEM/NSC109555 combination significantly increased the level of intracellular reactive oxygen species (ROS), accompanied by induction of apoptotic cell death. Inhibition of ROS generation by N-acetyl cysteine (NAC) significantly reversed the effect of GEM/NSC109555 in apoptosis and cytotoxicity. Furthermore, genetic knockdown of CHK2 by siRNA enhanced GEM-induced apoptotic cell death. These findings suggest that inhibition of CHK2 would be a beneficial therapeutic approach for pancreatic cancer therapy in clinical treatment.

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[229]

TÍTULO / TITLE: - WNT5A/JNK signaling regulates pancreatic cancer cells migration by Phosphorylating Paxillin.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Jul-Aug;13(4):384-92. doi: 10.1016/j.pan.2013.05.008. Epub 2013 Jun 10.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.05.008

AUTORES / AUTHORS: - Wei W; Li H; Li N; Sun H; Li Q; Shen X

INSTITUCIÓN / INSTITUTION: - School of Medicine, Nankai University, Tianjin 300071, China.

RESUMEN / SUMMARY: - BACKGROUND: Expression of WNT5A associated with aggressive tumor biology and poor clinical outcome of various types of cancer. However its function in the metastasis property of pancreatic cells still needs to be elucidated. METHODS: We detected the expressions of WNT5A, JNK1/p-JNK1 and Paxillin/p-Paxillin in cancer and the para-carcinoma tissues of

pancreatic cancer. To understand how WNT5A/JNK signaling affects pancreatic cancer cell migration through the phosphorylation of cellular substrates of Paxillin, In vitro, we knocked down the WNT5A in PANC1, Capan-2 and HT1080 cell lines, and then tested the expression of JNK1. We detected the proteins of phosphorylation of Paxillin after JNK1 was inhibited and then the cells migration assay was evaluated. Moreover, JNK1 functionally phosphorylates serine178 on paxillin in vitro was detected .At last we subsequently observed whether WNT5A/JNK signaling modulates some molecule expressions relevant to focal adhesion (FA) formation and mesenchymal transition (EMT) and cell cycle. RESULTS: WNT5A, p-JNK1 and p-Paxillin were highly expressed in early stage of tumor tissues. In vitro, WNT5A/JNK signaling promotes cell migration in pancreatic cancer by phosphorylating serine178 on Paxillin, an FA adaptor, which means WNT5A may regulate FA's function.WNT5A up-regulates the molecule's expressions relevant to cell adhesion through the phosphorylation of JNK1, including MMP1, MMP2, ICAM and CD44. In addition, WNT5A/JNK signaling promoted the mRNA expressions of vimentin, but decreased in E-Cadherin expression, which suggested its regulatory effects on the EMT processes. WNT5A/JNK signaling didn't modulate cell proliferation. CONCLUSION: WNT5A/JNK signaling initiate cell migration of pancreatic cancer through activation of Paxillin, which suggested WNT5A has the potency of being an effective therapeutic target for the metastasis of pancreatic cancer.

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[230]

TÍTULO / TITLE: - Hedgehog signaling regulates hypoxia induced epithelial to mesenchymal transition and invasion in pancreatic cancer cells via a ligand-independent manner.

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

REVISTA / JOURNAL: - Mol Cancer. 2013 Jun 20;12:66. doi: 10.1186/1476-4598-12-66.

●● Enlace al texto completo (gratuito o de pago) 1186/1476-4598-12-66

AUTORES / AUTHORS: - Lei J; Ma J; Ma Q; Li X; Liu H; Xu Q; Duan W; Sun Q; Xu J; Wu Z; Wu E

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, First Affiliated Hospital of Medical College, Xi'an Jiaotong University, 277 West Yanta Road, Xi'an 710061Shaanxi Province, China. qyma56@mail.xjtu.edu.cn.

RESUMEN / SUMMARY: - BACKGROUND: Hypoxia plays a vital role in cancer epithelial to mesenchymal transition (EMT) and invasion. However, it is not quite clear how hypoxia may contribute to these events. Here we investigate the role of Hedgehog (Hh) signaling in hypoxia induced pancreatic cancer EMT and invasion. METHODS: Pancreatic cancer cells were cultured under controlled hypoxia conditions (3% O2) or normoxic conditions. HIF-1alpha siRNA, cyclopamine (a SMO antagonist) and GLI1 siRNA were used to inhibit HIF-

1alpha transcription or Hh signaling activation. The effect of hypoxia and Hh signaling on cancer cell EMT and invasion were evaluated by Quantitative real-time PCR analysis, Western blot analysis and invasion assay. RESULTS: Here, we show that non-canonical Hh signaling is required as an important role to switch on hypoxia-induced EMT and invasion in pancreatic cancer cells. Moreover, our data demonstrate hypoxia induces EMT process as well as invasion, and activates the non-canonical Hh pathway without affecting sonic hedgehog homolog (SHH) expression. Moreover, these effects are reversible upon HIF-1alpha siRNA interference with unchanged SHH and patched1 (PTCH1) level. Furthermore, our data demonstrate that hypoxia induced invasion and EMT process are effectively inhibited by Smoothened (SMO) antagonist cyclopamine and GLI1 siRNA. In addition, GLI1 interference inhibited EMT progress with significantly suppressed vimentin expression, whereas inhibition of SMO through cyclopamine could not reduce vimentin level. This data indicate that hypoxia could trigger other factors (such as TGF-beta, KRAS or RTK) bypassing SMO to activate GLI1 directly. CONCLUSIONS: Our findings suggest that Hh signaling modulates hypoxia induced pancreatic cancer EMT and invasion in a ligand-independent manner. Thus, Hh signaling may represent a promising therapeutic target for preventing pancreatic cancer progression.

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[231]

TÍTULO / TITLE: - Profilin1 sensitizes pancreatic cancer cells to irradiation by inducing apoptosis and reducing autophagy.

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

REVISTA / JOURNAL: - Curr Mol Med. 2013 Jun 28.

AUTORES / AUTHORS: - Cheng H; Li J; Liu C; Yao W; Xu Y; Frank TS; Cai X; Shi S; Lu Y; Qin Y; Liu L; Xu J; Long J; Ni QX; Li M; Yu X

INSTITUCIÓN / INSTITUTION: - The Vivian L. Smith Department of Neurosurgery, The University of Texas Medical School at Houston, Houston, Texas 77030, USA. Min.Li@uth.tmc.edu.

RESUMEN / SUMMARY: - Pancreatic cancer has an extremely poor prognosis mainly due to lack of effective treatment options. Radiotherapy is mostly applied to locally advanced cases, although tumor radioresistance limits the effectiveness. Profilin1, a novel tumor suppressor gene, was reported to be down-regulated in various cancers and associated with tumor progression. The objective of this study was to demonstrate how profilin1 affected pancreatic cancer radiosensitivity. We showed profilin1 was down-regulated in pancreatic cancer cells after exposure to radiation, and re-expression of profilin1 suppressed tumor cell viability and increased DNA damage following irradiation. Further studies revealed that up-regulation of profilin1 facilitated apoptosis and repressed autophagy induced by irradiation, which might sensitize pancreatic

cancer cells to radiation treatment. Our findings may provide a novel therapeutic strategy for sensitizing pancreatic cancer to radiotherapy.

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[232]

TÍTULO / TITLE: - Pancreatic ductal adenocarcinomas with multiple large cystic structures: A clinicopathologic and immunohistochemical study of seven cases.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Jul-Aug;13(4):401-8. doi: 10.1016/j.pan.2013.05.004. Epub 2013 May 21.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.05.004

AUTORES / AUTHORS: - Nitta T; Mitsuhashi T; Hatanaka Y; Hirano S; Matsuno Y

INSTITUCIÓN / INSTITUTION: - Department of Surgical Pathology, Hokkaido University Hospital, Sapporo, Hokkaido, Japan; Department of Surgical Oncology, Division of Cancer Medicine, Hokkaido University Graduate School of Medicine, Sapporo, Hokkaido, Japan.

RESUMEN / SUMMARY: - BACKGROUND/OBJECTIVES: Pancreatic ductal adenocarcinoma (PDA) with cystic change is classified into several types according to the features of the cysts; however, those tumors do not constitute a uniform group, and the classification is controversial. In this study, we have described a series of cystic PDAs that show distinctive and previously unreported morphologic and immunohistochemical features. METHODS: We analyzed 200 cases of PDA treated surgically at a single institution, and extracted the clinical and histopathological features of 7 tumors showing multiple large cystic (MLC) structure. RESULTS: Preoperative radiographic images revealed a multilocular mass in the pancreas which was similar to intraductal papillary mucinous neoplasm or mucinous cystic neoplasm. These tumors were associated with more than 5 large cystic structures and numerous intratumoral microcysts lined by epithelial cells with various degrees of atypia. The average maximal diameter of the cysts (3.7 cm) was much larger than that of previously reported. Immunohistochemically, the cyst-lining epithelia were almost negative for mucin core protein (MUC) 1, MUC2, and MUC6, and showed only focal staining for MUC5AC. Maspin, CEA, and p53 were strongly positive, and the Ki-67 labeling index was high in both cells in solid areas and cyst-lining epithelia. CONCLUSION: We considered the MLC structures in PDA to be a mixture of ectatic neoplastic glands and retention cysts with ductal cancerization or pancreatic intraepithelial neoplasia (PanIN); however, they might represent a new entity of cystic PDA because of the unusually large size of the dilated cysts.

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[233]

TÍTULO / TITLE: - Quantitative analysis of VEGF-C mRNA of extrahepatic cholangiocarcinoma with real-time PCR using samples obtained during endoscopic retrograde cholangiopancreatography.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Scand J Gastroenterol. 2013 Jul;48(7):848-55. doi: 10.3109/00365521.2013.800990. Epub 2013 May 31.
●● Enlace al texto completo (gratuito o de pago)
3109/00365521.2013.800990
AUTORES / AUTHORS: - Dobashi A; Imazu H; Tatsumi N; Okabe M; Ang TL; Tajiri H
INSTITUCIÓN / INSTITUTION: - Department of Endoscopy, The Jikei University School of Medicine , Tokyo , Japan.
RESUMEN / SUMMARY: - Abstract Objective. Vascular endothelial growth factor (VEGF)-C overexpression in extrahepatic cholangiocarcinoma (ECC) has been shown to be correlated with lymph node metastasis. The intensity of immunohistochemical staining of VEGF-C protein in surgical samples has been used as index of VEGF-C overexpression in previous studies. The aim of the study was to examine if VEGF-C overexpression in ECC could be preoperatively detected by using samples obtained during ERCP. Methods. Consecutive patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) for biliary stricture during the study period were prospectively analyzed. VEGF-C mRNA was quantified by real-time PCR methods using endoscopic samples obtained during ERCP. The high intensity of immunohistochemical staining of VEGF-C protein in surgical samples was used for the reference standard of VEGF-C overexpression. The level of S100P mRNA which was a novel diagnostic marker of ECC was also quantified to evaluate whether the endoscopic samples contained ECC cells. Results. Twenty-five patients were enrolled in this study. Eighteen patients were diagnosed as ECC and seven patients were diagnosed as benign biliary structure. Nine of eighteen patients with ECC, who showed positive S100P mRNA in endoscopic samples and received surgical resection, were finally analyzed. Receiver operating characteristics analysis yielded VEGF-C mRNA cut-off value of 3.85 for detection of VEGF-C overexpression, and the diagnostic performance of VEGF-C mRNA measurement in the endoscopic sample for VEGF-C overexpression reached sensitivity of 75.0%, specificity of 100%, and accuracy of 88.9%. Conclusion. The quantification of VEGF-C mRNA of ECC with real-time PCR using endoscopic samples was useful for preoperative detection of VEGF-C overexpression.

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[234]
TÍTULO / TITLE: - Effect of 3D matrix compositions on the efficacy of EGFR inhibition in pancreatic ductal adenocarcinoma cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Biomacromolecules. 2013 Jul 27.

●● Enlace al texto completo (gratuito o de pago) 1021/bm4004496

AUTORES / AUTHORS: - Ki CS; Shih H; Lin CC

RESUMEN / SUMMARY: - Therapeutics to inhibit signaling of epidermal growth factor receptor (EGFR) has been suggested as a potential treatment for pancreatic cancers and two-dimensional (2D) cell culture techniques are commonly used to identify and/or verify the therapeutic efficacy of EGFR inhibitors. However, drug targets identified from conventional cell culture techniques may not exhibit desired functions when these drugs were tested in animal studies, in large part due to the complicated tumor microenvironments. Hence, it is crucial to develop a biomimetic cell culture system capable of recapitulating aspects of tumor niches for studying cancer cell fate processes under the influence of various environmental stimuli. In this study, we utilized a versatile PEG-peptide hydrogel system to demonstrate the influence of matrix properties and EGFR inhibition on the growth of a pancreatic ductal adenocarcinoma cell line (PANC-1). PANC-1 cells were encapsulated in 8-arm PEG-norbornene (PEG8NB) hydrogels cross-linked by matrix metalloproteinase (MMP) sensitive peptide (MMPLinker) using thiol-ene photo-click chemistry. In soft hydrogels (G'~2 kPa), cells retained high initial viability and formed clusters after pro-longed culture, whereas cells encapsulated in stiff hydrogels (G'~12 kPa) exhibited lower initial viability and reduced proliferation. While the immobilization of an EGFR peptide inhibitor, Asn-Tyr-Gln-Gln-Asn or NYQQN, in soft hydrogels did not cause cell death, this peptide induced significant cell apoptosis when immobilized in stiff hydrogels. Western blotting results showed that cell death was due to reduced expression of EGFR and Akt in stiff hydrogels under the influence of immobilized NYQQN peptide. These results shed light on the importance and non-negligible role of matrix properties on the efficacy of anti-tumor drugs.

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[235]

TÍTULO / TITLE: - cAMP inhibits migration, ruffling and paxillin accumulation in focal adhesions of pancreatic ductal adenocarcinoma cells: Effects of PKA and EPAC.

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

REVISTA / JOURNAL: - Biochim Biophys Acta. 2013 Jun 22. pii: S0167-4889(13)00234-6. doi: 10.1016/j.bbamcr.2013.06.011.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bbamcr.2013.06.011

AUTORES / AUTHORS: - Burdyga A; Conant A; Haynes L; Zhang J; Jalink K; Sutton R; Neoptolemos J; Costello E; Tepikin A

INSTITUCIÓN / INSTITUTION: - Department of Cellular and Molecular Physiology, The University of Liverpool, Crown Street, Liverpool L69 3BX, UK.

RESUMEN / SUMMARY: - We demonstrated that increasing intracellular cAMP concentrations result in the inhibition of migration of PANC-1 and other pancreatic ductal adenocarcinoma (PDAC) cell types. The rise of cAMP was accompanied by rapid and reversible cessation of ruffling, by inhibition of focal adhesion turnover and by prominent loss of paxillin from focal adhesions. All these phenomena develop rapidly suggesting that cAMP effectors have a direct influence on the cellular migratory apparatus. The role of two primary cAMP effectors, exchange protein activated by cAMP (EPAC) and protein kinase A (PKA), in cAMP-mediated inhibition of PDAC cell migration and migration-associated processes was investigated. Experiments with selective activators of EPAC and PKA demonstrated that the inhibitory effect of cAMP on migration, ruffling, focal adhesion dynamics and paxillin localisation is mediated by PKA, whilst EPAC potentiates migration.

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[236]

TÍTULO / TITLE: - Treatment of Borderline Resectable Pancreatic Cancer.

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

REVISTA / JOURNAL: - Curr Treat Options Oncol. 2013 Jun 21.

●● Enlace al texto completo (gratuito o de pago) 1007/s11864-013-0244-6

AUTORES / AUTHORS: - Cooper AB; Tzeng CW; Katz MH

INSTITUCIÓN / INSTITUTION: - MD Anderson Cancer Center, 1400 Pressler Dr., Houston, TX, USA.

RESUMEN / SUMMARY: - OPINION STATEMENT: Borderline resectable pancreatic adenocarcinoma represents a subset of localized cancers that are at high risk for a margin-positive resection and early treatment failure when resected de novo. Although several different anatomic definitions for this disease stage exist, there is agreement that some degree of reconstructible mesenteric vessel involvement by the tumor is the critical anatomic feature that positions borderline resectable between anatomically resectable and unresectable (locally advanced) tumors in the spectrum of localized disease. Consensus also exists that such cancers should be treated with neoadjuvant chemotherapy and/or chemoradiation before resection; although the optimal algorithm is unknown, systemic chemotherapy followed by chemoradiation is a rational approach. Although gemcitabine-based systemic chemotherapy with either 5-FU or gemcitabine-based chemoradiation regimens has been used to date, newer regimens, including FOLFIRINOX, should be evaluated on protocol. Delivery of neoadjuvant therapy necessitates durable biliary decompression for as many as 6 months in many patients with cancers of the pancreatic head. Patients with no evidence of metastatic disease following neoadjuvant therapy should be brought to the operating room for pancreatectomy, at which time resection of the superior mesenteric/portal vein and/or hepatic artery should be performed when necessary to achieve a margin-negative resection. Following

completion of multimodality therapy, patients with borderline resectable pancreatic cancer can expect a duration of survival as favorable as that of patients who initially present with resectable tumors. Coordination among a multidisciplinary team of physicians is necessary to maximize these complex patients' short- and long-term oncologic outcomes.

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[237]

TÍTULO / TITLE: - Prospects of miRNA-Based Therapy for Pancreatic Cancer.

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

REVISTA / JOURNAL: - Curr Drug Targets. 2013 Sep;14(10):1101-9.

AUTORES / AUTHORS: - Pai P; Rachagani S; Are C; Batra SK

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, 985870 Nebraska Medical Center, Omaha, NE 68198-5870, USA. sbatra@unmc.edu.

RESUMEN / SUMMARY: - Pancreatic cancer (PC) is the fourth leading cause of cancer related deaths in the U.S., with a less than 6% five-year survival rate. Treatment is confounded by advanced stage of disease at presentation, frequent metastasis to distant organs at the time of diagnosis and resistance to conventional chemotherapy. In addition, the molecular pathogenesis of the disease is unclear. The extensive study of miRNAs over the past several years has revealed that miRNAs are frequently de-regulated in pancreatic cancer and contribute to the pathogenesis and aggressiveness of the disease. Several studies have tackled the practical difficulties in the application of miRNAs as viable therapeutic and diagnostic tools. Given that a single miRNA can affect a myriad of cellular processes, successful targeting of miRNAs as therapeutic agents could likely yield dramatic results. The current review attempts to summarize the advances in the field and assesses the prospects for miRNA profiling and targeting in aiding PC treatment.

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[238]

TÍTULO / TITLE: - Searching for clinical and economic value in pancreatic cancer.

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

REVISTA / JOURNAL: - Am J Manag Care. 2013 Mar-Apr;19(3 Spec No.):SP.

AUTORES / AUTHORS: - Zimmerman MP; Mehr SR

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[239]

TÍTULO / TITLE: - Evaluating the Utility of Existing Patient-Reported Outcome Scales in Novel Patient Populations with Pancreatic Cancer, Lung Cancer, and Myeloproliferative Neoplasms Using Medicare Current Beneficiary Survey Data.

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

REVISTA / JOURNAL: - Patient. 2013 Jul 5.

●● Enlace al texto completo (gratuito o de pago) 1007/s40271-013-0018-z

AUTORES / AUTHORS: - Ivanova JI; Mytelka DS; Duh MS; Birnbaum HG; Cummings AK; San Roman AM; Price GL; Swindle RW

INSTITUCIÓN / INSTITUTION: - Analysis Group, Inc., New York, NY, USA.

RESUMEN / SUMMARY: - BACKGROUND: While there are validated patient-reported outcomes (PRO) instruments for use in specific cancer populations, no validated general instruments exist for use in conditions common to multiple cancers, such as muscle wasting and consequent physical disability. The Medicare Current Beneficiary Survey (MCBS), a survey in a nationally representative sample of Medicare beneficiaries, includes items from three well known scales with general applicability to cancer patients: Katz activities of daily living (ADL), Rosow-Breslau instrumental ADL (IADL), and a subset of physical performance items from the Nagi scale. OBJECTIVE: This study evaluated properties of the Katz ADL, Rosow-Breslau IADL, and a subset of the Nagi scale in patients with pancreatic cancer, lung cancer, and myeloproliferative neoplasms (MPN) using data from MCBS linked with Medicare claims in order to understand the potential utility of the three scales in these populations; understanding patient-perceived significance was not in scope. METHODS: The study cohorts included Medicare beneficiaries aged >/=65 years as of 1 January of the year of their first cancer diagnosis with one or more health assessments in a community setting in the MCBS Access to Care data from 1991 to 2009. Beneficiaries had at least two diagnoses in de-identified Medicare claims data linked to the MCBS for one of the following cancers: pancreatic, lung, or MPN. The Katz ADL, Rosow-Breslau IADL, and Nagi scales were calculated to assess physical functioning over time from cancer diagnosis. Psychometric properties for each scale in each cohort were evaluated by testing for internal consistency, test-retest reliability, and responsiveness by comparing differences in mean scale scores over time as cancer progresses, and differences in mean scale scores before and after hospitalization (for lung cancer cohort). RESULTS: The study cohorts included 90 patients with pancreatic cancer, 863 with lung cancer, and 135 with MPN. Among each cancer cohort, the Katz ADL, Rosow-Breslau IADL, and Nagi scales had acceptable internal consistency (Cronbach's alpha generally between 0.70 and 0.90) and test-retest reliability for consecutive surveys before diagnosis and consecutive surveys after diagnosis (when patients' functioning was more stable). Compared with mean scale scores at the survey 1-2 years before cancer diagnosis (baseline), mean scale scores at the first survey after cancer diagnosis were significantly higher ($P < 0.05$), indicating worsening, for Katz ADL, Rosow-Breslau IADL, and Nagi scales (items scored 0-1) (0.54 vs. 1.45, 1.15 vs. 2.20, and 2.29 vs. 3.08, respectively, for pancreatic cancer; 0.73 vs. 1.24, 1.29 vs. 2.01, and 2.41 vs. 2.85 for lung cancer; and 0.44 vs. 0.86, 0.87 vs. 1.36, and 1.87 vs. 2.32 for MPN). Among lung cancer patients, scale scores increased significantly

following a hospitalization, suggesting a worsening of functional status. CONCLUSIONS: The Katz ADL, Rosow-Breslau IADL, and Nagi scales collected in the MCBS demonstrate acceptable internal consistency and test-retest reliability among patients with pancreatic cancer, lung cancer, and MPN, and are consistent with clinical worsening following diagnosis or hospitalization. These results suggest that using retrospective data may allow researchers to conduct preliminary assessments of existing PRO instruments in new populations of interest and generate useful exploratory disease information before embarking on de novo PRO development.

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[240]

TÍTULO / TITLE: - Intraductal oncocytic papillary neoplasm: A rare pancreatic mass.

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

REVISTA / JOURNAL: - Can J Gastroenterol. 2013 Jul;27(7):387-8.

AUTORES / AUTHORS: - Brahmania M; Khangura D; Cantor M

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[241]

TÍTULO / TITLE: - Calix[6]arene bypasses human pancreatic cancer aggressiveness: Downregulation of receptor tyrosine kinases and induction of cell death by reticulum stress and autophagy.

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

REVISTA / JOURNAL: - Biochim Biophys Acta. 2013 Jul 19. pii: S0167-4889(13)00283-8. doi: 10.1016/j.bbamcr.2013.07.010.

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

1016/j.bbamcr.2013.07.010

AUTORES / AUTHORS: - Pelizzaro-Rocha KJ; de Jesus MB; Ruela-de-Sousa RR; Nakamura CV; Reis FS; de Fatima A; Ferreira-Halder CV

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry, Biology Institute, University of Campinas, Campinas, Sao Paulo, Brazil.

RESUMEN / SUMMARY: - Pancreatic cancer ranks fourth among cancer-related causes of death in North America. Minimal progress has been made in the diagnosis and treatment of patients with late-stage tumors. Moreover, pancreatic cancer aggressiveness is closely related to high levels of pro-survival mediators, which can ultimately lead to rapid disease progression, resistance and metastasis. The main goal of this study was to define the mechanisms by which calix[6]arene (CLX6), but not other calixarenes, efficiently decreases the aggressiveness of a drug resistant human pancreas carcinoma cell line (Panc-1). CLX6 was more potent in reducing Panc-1 cell viability than gemcitabine and 5-fluorouracil. In relation to the underlying mechanisms of cytotoxic effects, CLX6 led to cell cycle arrest in the G0/G1 phase through downregulation of PIM1, CDK2, CDK4 and retinoblastoma proteins. Importantly, CLX6 abolished signal transduction of Mer and AXL tyrosine kinase receptors,

both of which are usually overexpressed in pancreatic cancer. Accordingly, inhibition of PI3K and mTOR was also observed, and these proteins are positively modulated by Mer and AXL. Despite decreasing the phosphorylation of AKT at Thr308, CLX6 caused an increase in phosphorylation at Ser473. These findings in conjunction with increased BiP and IRE1-alpha provide a molecular basis explaining the capacity of CLX6 to trigger endoplasmic reticulum stress and autophagic cell death. Our findings highlight CLX6 as a potential candidate for overcoming pancreatic cancer aggressiveness. Importantly, we provide evidence that CLX6 affects a broad array of key targets that are usually dysfunctional in pancreatic cancer, a highly desirable characteristic for chemotherapeutics.

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[242]

TÍTULO / TITLE: - Pancreatic adenocarcinoma: general histological overview.

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

REVISTA / JOURNAL: - Acta Chir Belg. 2013 Mar-Apr;113(2):71-6.

AUTORES / AUTHORS: - Demetter P; D'Haene N; Verset L; Nagy N

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Erasme University Hospital, Universite Libre de Bruxelles (ULB), Belgium. pieter.demetter@erasme.ulb.ac.be

RESUMEN / SUMMARY: - In Belgium, approximately 1100 new cases of pancreatic ductal adenocarcinoma are diagnosed each year. Although in the last twenty years several advances have been registered in the field of pancreatic pathology, few therapies are efficacious, and it remains one of the deadliest of all cancers. Histological variants with a somewhat different prognosis have been recognised, and precursor lesions identified. This article reviews the histological aspects of ductal adenocarcinoma, its variants and the precursor lesions. Study and knowledge of these precursor lesions offers the best hope for treating pancreatic cancer before an incurable invasive tumour develops.

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[243]

TÍTULO / TITLE: - Pancreatic Neuroendocrine Tumor in a Child with a Tuberous Sclerosis Complex 2 (TSC2) Mutation.

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

REVISTA / JOURNAL: - Endocr Pract. 2013 Jun 11:1-16.

●● Enlace al texto completo (gratuito o de pago) 4158/EP13010.CR

AUTORES / AUTHORS: - Bombardieri R; Moavero R; Roberto D; Cerminara C; Curatolo P

INSTITUCIÓN / INSTITUTION: - Neuroscience Department, Pediatric Neurology Unit, Tor Vergata University Hospital of Rome, Italy.

RESUMEN / SUMMARY: - Objective: Pancreatic neuroendocrine tumors (PanNETs) are rare in children with tuberous sclerosis complex (TSC). The objective of this report is to describe a case of PanNET in a boy with TSC.Methods: We describe the patient's clinical presentation, biochemical workup and laboratory tests.Results: A 10-year-old boy with a TSC2 mutation presented with a non-secretory PanNET discovered during routine annual abdominal ultrasound. Surgical distal pancreatectomy with spleen preservation was undertaken. The excised tumor appeared nodular, whitish and encapsulated. The tumor was composed of pancreatic endocrine monomorphic cells and the solid appearance of the tumor was interrupted by areas of cycstic degeneration. Mitoses were rare; the proliferation index was estimated around 4%. Local lymph nodes showed hyperplasia but were free of metastatic disease. Immunohistochemical examinations were positive for the neuroendocrine markers chromogranin, neurospecific enolase, synaptophysin, CAM52 and vimentin and were negative for CD10 and alpha-1 antitrypsin. The immunohistochemistry also showed a lack of hyperactivation of mTOR pathway. All data supported the diagnosis of a grade II well-differentiated neuroendocrine neoplasm, according to WHO (World Health Organization).Conclusions: Thirteen non-secretory PanNET cases associated with TSC have been reported, including our patient (9M and 4F; 7 with TSC2 mutation). These tumors are usually asymptomatic and can be associated with metastasis; therefore early diagnosis is crucial for prompt treatment. It is still unclear whether PanNETs should be considered a feature of TSC. However due to this association, we suggest that pancreas investigation should be included in routine examinations in males with TSC2 mutation.

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[244]

TÍTULO / TITLE: - Considerations for the prediction of survival time in pancreatic cancer based on registry data.

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

REVISTA / JOURNAL: - J Pharmacokinet Pharmacodyn. 2013 Aug;40(4):527-36. doi: 10.1007/s10928-013-9327-z. Epub 2013 Jul 12.

●● Enlace al texto completo (gratuito o de pago) 1007/s10928-013-9327-z

AUTORES / AUTHORS: - Bajaj G; Dombrowsky E; Yu Q; Agarwal B; Barrett JS

INSTITUCIÓN / INSTITUTION: - Laboratory of Applied PK/PD, Department of Clinical Pharmacology and Therapeutics, The Children's Hospital of Philadelphia, Colket Translational Research Building, Room 4012, 3501 Civic Center Blvd, Philadelphia, PA, 19104, USA.

RESUMEN / SUMMARY: - Semi-parametric and parametric survival models in patients with pancreatic adenocarcinoma (PC) using data from Surveillance, Epidemiology, and End Result (SEER) registry were developed to identify relevant covariates affecting survival, verify against external patient data and

predict disease outcome. Data from 82,251 patients was extracted using site and histology codes for PC in the SEER database and refined based on specific cause of death. Predictors affecting survival were selected from SEER database; the analysis dataset included 2,437 patients. Survival models were developed using both semi-parametric and parametric approaches, evaluated using Cox-Snell and deviance residuals, and predictions were assessed using an external dataset from Saint Louis University (SLU). Prediction error curves (PECs) were used to evaluate prediction performance of these models compared to Kaplan-Meier response. Median overall survival time of patients from SEER data was 5 months. Our analysis shows that the PC data from SEER was best fitted by both semi-parametric and the parametric model with log-logistic distribution. Predictors that influence survival included disease stage, grade, histology, tumor size, radiation, chemotherapy, surgery, and lymph node status. Survival time predictions from the SLU dataset were comparable and PECs show that both semi-parametric and parametric models exhibit similar predictive performance. PC survival models constructed from registry data can provide a means to classify patients into risk-based subgroups, to predict disease outcome and aide in the design of future prospective randomized trials. These models can evolve to incorporate predictive biomarker and pharmacogenetic correlates once adequate causal data is established.

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[245]

TÍTULO / TITLE: - Potential epigenetic biomarkers for the diagnosis and prognosis of pancreatic ductal adenocarcinomas.

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

REVISTA / JOURNAL: - Expert Rev Mol Diagn. 2013 Jun;13(5):431-43. doi: 10.1586/erm.13.38.

●● Enlace al texto completo (gratuito o de pago) 1586/erm.13.38

AUTORES / AUTHORS: - Hinton J; Callan R; Bodine C; Glasgow W; Brower S; Jiang SW; Li J

INSTITUCIÓN / INSTITUTION: - School of Medicine, Mercer University, Savannah, GA 31404, USA.

RESUMEN / SUMMARY: - With an estimated 37,000 deaths per year, pancreatic cancer is the fourth leading cause of cancer deaths in the USA. A total of 95% of pancreatic cancers are exocrine neoplasms, known as pancreatic ductal adenocarcinomas (PDACs). The difficulty of early diagnosis and the high prevalence of metastasis associated with PDAC contribute to its dismal prognosis. The past decade has witnessed intensive study and impressive progress in searching for more sensitive, specific and cost-effective biomarkers. This review focuses on the epigenetic biomarkers potentially useful for the management of PDAC. The authors begin with an overview on the available biomarkers, and subsequently discuss the recent development in epigenetic

biomarkers, including DNA methylation, miRNA and histone modifications in diversified specimens of cell lines, xenograft, cancer tissues, pancreatic juice and patient blood. These findings raise the possibility for clinical application of epigenetic biomarkers towards screening, early diagnosis, prognosis, chemosensitivity prediction and recurrence surveillance of PDAC patients.

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[246]

TÍTULO / TITLE: - aPKClambda/iota is a beneficial prognostic marker for pancreatic neoplasms.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Jul-Aug;13(4):360-8. doi: 10.1016/j.pan.2013.05.006. Epub 2013 May 22.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.05.006

AUTORES / AUTHORS: - Kato S; Akimoto K; Nagashima Y; Ishiguro H; Kubota K; Kobayashi N; Hosono K; Watanabe S; Sekino Y; Sato T; Sasaki K; Nakaigawa N; Kubota Y; Inayama Y; Endo I; Ohno S; Maeda S; Nakajima A

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

RESUMEN / SUMMARY: - Pancreatic cancer is a lethal disease. Overall survival is typically 6 months from diagnosis. Determination of prognostic factors in pancreatic cancer that would allow identification of patients who could potentially benefit from aggressive treatment is important. However, until date, there are no established reliable prognostic factors for pancreatic cancer patients. Herein, we propose a beneficial biomarker which is significantly correlated with the prognosis in pancreatic cancer patients. Atypical protein kinase C lambda/iota (aPKClambda/iota) is overexpressed and has been implicated in the progression of several cancers. We tested the expression levels of aPKClambda/iota in two types of pancreatic neoplasm, pancreatic ductal adenocarcinoma (PDAC) and intraductal papillary mucinous neoplasms (IPMNs), by immunohistochemistry. Examination of the aPKClambda/iota expression levels in surgically resected specimens of PDCA (n = 115) demonstrated that the expression levels of aPKClambda/iotain PDAC had prognostic implications, independent of the Tumor-Node-Metastasis classification and World Health Organization tumor grade. In the case of IPMNs (n = 46) also, the expression levels of aPKClambda/iotain IPMN were found to be of prognostic importance, independent of the World Health Organization histological grade or morphological type. Interestingly, high expression levels of aPKClambda/iota were significantly correlated with a worse histological grade (p = 0.010) and advanced stage of the tumor (p = 0.0050) in IPMN patients. These findings suggest that high expression levels of aPKClambda/iota could be involved in the malignant transformation of IPMNs. Based on these observations, we propose the expression level of aPKClambda/iota as a prognostic marker common to different types of pancreatic neoplasms.

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[247]

TÍTULO / TITLE: - Solid and cystic pseudopapillary tumor of the pancreas: A case report.

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

REVISTA / JOURNAL: - Srp Arh Celok Lek. 2013 May-Jun;141(5-6):384-6.

AUTORES / AUTHORS: - Milojevic BZ; Markovic RM; Cvetkovic AM

INSTITUCIÓN / INSTITUTION: - Department of Gastrointestinal Surgery, Clinic for Surgery, Clinical Center Kragujevac, Kragujevac, Serbia.

RESUMEN / SUMMARY: - INTRODUCTION: Solid and cystic pseudopapillary tumor of the pancreas is a rare tumor of the pancreas, for the first time described by Frantz et al. in 1959. The majority of patients are young females and most of them are asymptomatic. CASE OUTLINE: We report a case of 25-year old woman who was admitted to our institution with abdominal pain and a palpable mass in the left hypochondrial area. US and CT scan revealed a solid and cystic pseudopapillary tumor in the head of the pancreas. The patient was treated by Whipple procedure, modification Longmire-Traverso. There was no metastatic disease either in the liver or peritoneum. Histologically the tumor was diagnosed as a solid and cystic pseudopapillary tumor of the pancreas. CONCLUSION: The unclear pre-operative diagnoses, together with incidence of potential malignancy as well as good outcome with resection, suggest that all suspected cystic tumors of the pancreas should be resected.The exact diagnosis is based on histological findings.

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[248]

TÍTULO / TITLE: - Advanced EUS imaging for early detection of pancreatic cancer.

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

REVISTA / JOURNAL: - Gastrointest Endosc Clin N Am. 2013 Jul;23(3):607-23. doi: 10.1016/j.giec.2013.03.001. Epub 2013 May 3.

●● Enlace al texto completo (gratuito o de pago) 1016/j.giec.2013.03.001

AUTORES / AUTHORS: - Amin S; Dimaio CJ; Kim MK

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology, Department of Medicine, Mount Sinai School of Medicine, 5 East 98th Street, 11th Floor, New York, NY 10029, USA.

RESUMEN / SUMMARY: - Endoscopic ultrasound (EUS)-fine needle aspiration remains the gold standard for diagnosing pancreatic malignancy. However, in a subset of patients, limitations remain in regards to image quality and diagnostic yield of biopsies. Several new devices and processors have been developed that allow for enhancement of the EUS image. Initial studies of these modalities do show promise. However, cost, availability, and overall incremental benefit to EUS-fine needle aspiration have yet to be determined.

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[249]

TÍTULO / TITLE: - miRNAs in Insulin Resistance and Diabetes-Associated Pancreatic Cancer: The 'Minute and Miracle' Molecule Moving as a Monitor in the 'Genomic Galaxy'.

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

REVISTA / JOURNAL: - Curr Drug Targets. 2013 Sep;14(10):1110-7.

AUTORES / AUTHORS: - Chakraborty C; George Priya Doss C; Bandyopadhyay S

INSTITUCIÓN / INSTITUTION: - Department of Bioinformatics, School of Computer and Information Sciences, Galgotias University, Greater Noida, India. drchiranjib@yahoo.com.

RESUMEN / SUMMARY: - The predominance of insulin resistance, T2D linked pancreatic cancer has increased throughout the world. The insulin/IGF signaling pathway related to insulin resistance, T2D and pancreatic cancer has been described. In this context, we have demonstrated the role of miRNAs in cancer progression and control of miRNAs in insulin/IGF signaling pathway, and pancreatic cancer. In this paper, an overview was depicted about the role of following miRNAs in pancreatic development and insulin secretion (miR-375, miR-7, miR-124ª2, miR-195, miR-126, miR-9, miR-96, miR-34ª); insulingrowth factor-1 receptor expression (miR-7, miR-139, miR-145, miR-1); the diabetes-associated pancreatic cancer pathway genes such as IRS, PI3K, AKT/PKB (miR-128ª, miR-19ª, miR-21, miR-29 a/b/c); mTOR protein regulation (miR- 99, miR-21, miR-126, and miR-146ª) etc. At last, we have also explained the role of miRNAs in diagnostic marker (miR- 200, miR-21, miR-103, miR-107, and miR-155) and as a therapeutic modulator (miR-34, miR-21, miR-221, and miR-101) in pancreatic cancer.

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[250]

TÍTULO / TITLE: - Iron chelation: inhibition of key signaling pathways in the induction of the epithelial mesenchymal transition in pancreatic cancer and other tumors.

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

REVISTA / JOURNAL: - Crit Rev Oncog. 2013;18(5):409-34.

AUTORES / AUTHORS: - Richardson A; Kovacevic Z; Richardson DR

INSTITUCIÓN / INSTITUTION: - Iron Metabolism and Chelation Program, Department of Pathology and Bosch Institute, University of Sydney, Sydney, New South Wales, 2006, Australia.

RESUMEN / SUMMARY: - Pancreatic cancer is the fourth leading cause of cancer-related deaths worldwide in both men and women. It presents late with non-specific symptoms, which makes it difficult to diagnose until the cancer has progressed and metastasized. Metastasis is facilitated by the epithelial-to-mes-

enchymal transition (EMT), which is promoted via the oncogenic transforming growth factor beta (TGFbeta), Wnt, and nuclear factor kappa B (NFkappaB) signaling pathways. However, recent studies have demonstrated that the EMT can be inhibited by novel anti-cancer agents known as thiosemicarbazone iron chelators. These novel agents also up-regulate the metastasis suppressor, N-myc downstream regulated gene 1 (NDRG1), which can restore normal signaling to the cell and suppresses metastasis via inhibition of the EMT. Through the ability of iron chelators to up-regulate NDRG1 expression and affect multiple molecular targets, these agents have the potential to maintain the epithelial phenotype of cancer cells and may lead to improved survival rates for patients with late-stage disease.

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[251]

TÍTULO / TITLE: - Calorie restriction delays the progression of lesions to pancreatic cancer in the LSL-KrasG12D; Pdx-1/Cre mouse model of pancreatic cancer.

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

REVISTA / JOURNAL: - Exp Biol Med (Maywood). 2013 Jul 4.

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

1177/1535370213493727

AUTORES / AUTHORS: - Lanza-Jacoby S; Yan G; Radice G; Lephong C; Baliff J; Hess R

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Thomas Jefferson University, Philadelphia, PA 19107, USA.

RESUMEN / SUMMARY: - Since pancreatic cancer is a lethal disease, developing prevention strategies is an important goal. We determined whether calorie restriction would prevent the development and delay progression of pancreatic intraepithelial neoplasms to pancreatic ductal adenocarcinoma (PDA) in LSL-KrasG12D/+; Pdx-1/Cre mice that develop all the precursor lesions that progress to PDA. Eight-week-old LSL-KrasG12D; Pdx-1/Cre mice were assigned to three groups: (1) ad libitum (AL) fed the AIN93M diet or (2) intermittently calorie restricted (ICR) a modified AIN93M at 50% of AL intake followed by one week intervals at 100% of AL intake, or (3) chronically calorie restricted (CCR) an AIN93M diet at 75% of AL intake. AL fed mice had a greater percentage of pancreatic ducts with PanIN-2 (13.6%) than did the ICR (1.0%) and CCR groups (1.6%), $P < 0.0001$. Calorie restriction (ICR [0%] and CCR [0.7%]) reduced the percentage of ducts with PanIN-3 lesions compared to the AL group (7.0%), $P < 0.0001$. The incidence of PanIN-2 or more lesions was significantly reduced in both ICR (27%; $n = 16$) and CCR (40%) mice ($n = 15$; $P < 0.001$) compared to AL (70%) fed mice ($n = 11$). The delayed progression of lesions in ICR and CCR mice was associated with reduced proliferation measured by proliferating cell nuclear antigen staining, reduced protein expression of Glut1, increased protein expression of Sirt1, increased serum

adiponectin, and decreased serum leptin. CCR resulted in decreased phosphorylated mammalian target of rapamycin and decreased serum insulin-like growth factor-1. In summary, this is the first study to show in LSL-KrasG12D; Pdx-1/Cre mice that ICR and CCR delay the progression of lesions to PDA.

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[252]

TÍTULO / TITLE: - Predictors of Recurrence in Intraductal Papillary Mucinous Neoplasm: Experience with 183 Pancreatic Resections.

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

REVISTA / JOURNAL: - J Gastrointest Surg. 2013 Jun 28.

●● Enlace al texto completo (gratuito o de pago) 1007/s11605-013-2242-1

AUTORES / AUTHORS: - Winner M; Epelboym I; Remotti H; Lee JL; Schrope BA; Chabot JA; Allendorf JD

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Columbia University Medical Center and the New York Presbyterian Hospital, New York, NY, USA.

RESUMEN / SUMMARY: - OBJECTIVES: We examined long-term outcomes in patients with surgically treated intraductal papillary mucinous neoplasm (IPMN) to determine if any clinical or histologic features could predict risk of recurrent disease. METHODS: We reviewed 183 margin-negative surgical resections performed for IPMN between 1994 and 2011 with documented postoperative abdominal imaging. We calculated time to recurrent disease as indicated by radiographic change and created a multivariable Cox proportional hazards model to assess the relationship between patient characteristics and histopathologic tumor features and disease recurrence. RESULTS: Among patients with margin-negative resections and adequate imaging follow-up, we observed a recurrence rate of 13 % over a median follow-up of 32.0 months. Individuals with invasive tumors on original pathology were more likely to recur (HR 5.2, 95 % CI 2.2-12.2); however, original pathology did not predict disease severity on recurrence. Controlling for invasive pathology, no other histologic feature of the original tumor, including dysplasia at the surgical margin, predicted recurrence. Among non-invasive IPMN, pancreatitis was associated with disease recurrence (HR 3.6, 95 % CI 1.2-10.7). CONCLUSIONS: The frequency of recurrent disease in this population and the inability to predict recurrence argues for universal and continuous surveillance after resection for IPMN. The relationship between pancreatitis and disease recurrence should be investigated further.

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[253]

TÍTULO / TITLE: - Necrolytic migratory erythema and glucagonoma rising from pancreatic head.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Pancreatology. 2013 Jul-Aug;13(4):455-7. doi: 10.1016/j.pan.2013.03.011. Epub 2013 Mar 30.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.03.011

AUTORES / AUTHORS: - Tseng HC; Liu CT; Ho JC; Lin SH
INSTITUCIÓN / INSTITUTION: - Department of Dermatology, Chang Gung Memorial Hospital - Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan.
RESUMEN / SUMMARY: - Glucagonoma syndrome encompasses necrolytic migratory erythema (NME), hyperglucagonemia, diabetes mellitus, anemia, weight loss, glossitis, angular cheilitis, steatorrhea, diarrhea, venous thrombosis, and neuropsychiatric disturbance. Of all the symptoms, NME is a rare skin disorder which is pathognomonic for glucagonoma. We present a 61-year-old woman diagnosed initially as pancreatic head adenocarcinoma with liver metastasis prior to the skin eruption. From the dermatologic finding and other clues, glucagonoma was diagnosed finally.

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[254]
TÍTULO / TITLE: - BIBF 1120 (nintedanib), a triple angiokinase inhibitor, induces hypoxia but not EMT and blocks progression of preclinical models of lung and pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Jun;12(6):992-1001. doi: 10.1158/1535-7163.MCT-12-0995. Epub 2013 May 31.

●● Enlace al texto completo (gratuito o de pago) 1158/1535-7163.MCT-12-0995

AUTORES / AUTHORS: - Kutluk Cenik B; Ostapoff KT; Gerber DE; Brekken RA
INSTITUCIÓN / INSTITUTION: - Hamon Center for Therapeutic Oncology Research, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA.
RESUMEN / SUMMARY: - Signaling from other angiokinases may underlie resistance to VEGF-directed therapy. We evaluated the antitumor and biologic effects of BIBF 1120 (nintedanib), a tyrosine kinase inhibitor that targets VEGF receptor, platelet-derived growth factor receptor, and fibroblast growth factor receptor in preclinical models of lung and pancreatic cancer, including models resistant to VEGF-targeted treatments. In vitro, BIBF 1120 did not show antiproliferative effects, nor did it sensitize tumor cells to chemotherapy. However, in vivo BIBF 1120 inhibited primary tumor growth in all models as a single agent and in combination with standard chemotherapy. Analysis of tumor tissue posttreatment revealed that BIBF 1120 reduced proliferation (phospho-histone 3) and elevated apoptosis (cleaved caspase-3) to a greater extent than chemotherapy alone. Furthermore, BIBF 1120 showed potent antiangiogenic effects, including decreases in microvessel density (CD31), pericyte coverage

(NG2), vessel permeability, and perfusion, while increasing hypoxia. Despite the induction of hypoxia, markers of epithelial-to-mesenchymal transition (EMT) were not elevated in BIBF 1120-treated tumors. In summary, BIBF 1120 showed potent antitumor and antiangiogenic activity in preclinical models of lung and pancreatic cancer where it induced hypoxia but not EMT. The absence of EMT induction, which has been implicated in resistance to antiangiogenic therapies, is noteworthy. Together, these results warrant further clinical studies of BIBF 1120.

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[255]

TÍTULO / TITLE: - miR-99b-targeted mTOR induction contributes to irradiation resistance in pancreatic cancer.

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

REVISTA / JOURNAL: - Mol Cancer. 2013 Jul 25;12(1):81.

●● Enlace al texto completo (gratuito o de pago) 1186/1476-4598-12-81

AUTORES / AUTHORS: - Wei F; Liu Y; Guo Y; Xiang A; Wang G; Xue X; Lu Z

RESUMEN / SUMMARY: - BACKGROUND: Radiation exerts direct antitumor effects and is widely used in clinics, but the efficacy is severely compromised by tumor resistance. Therefore uncovering the mechanism of radioresistance might promote the development of new strategies to overcome radioresistance by manipulating activity of the key molecules. METHODS: Immunohistochemistry were used to find whether mTOR were over-activated in radioresistant patients' biopsies. Then Western blot, real-time PCR and transfection were used to find whether radiotherapy regulates the expression and activity of mTOR by modulating its targeting microRNA in human pancreatic cancer cell lines PANC-1, Capan-2 and BxPC-3. Finally efficacy of radiation combined with mTOR dual inhibitor AZD8055 was assessed in vitro and in vivo. RESULTS: Ionizing radiation promoted mTOR expression and activation in pancreatic cancer cells through reducing miR-99b expression, which negatively regulated mTOR. Novel mTOR inhibitor, AZD8055 (10 nM, 100 nM, 500 nM) synergistically promoted radiation (0--10 Gy) induced cell growth inhibition and apoptosis. In human pancreatic cancer xenografts, fractionated radiation combined with AZD8055 treatment further increased the anti-tumor effect, the tumor volume was shrinked to 278 mm3 after combination treatment for 3 weeks compared with single radiation (678 mm3) or AZD8055 (708 mm3) treatment ($P < 0.01$). CONCLUSIONS: Our data provide a rationale for overcoming radio-resistance by combined with mTOR inhibitor AZD8055 in pancreatic cancer therapy.

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[256]

TÍTULO / TITLE: - Precancerous lesions of the pancreas.

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

REVISTA / JOURNAL: - Best Pract Res Clin Gastroenterol. 2013 Apr;27(2):299-322. doi: 10.1016/j.bpg.2013.04.001.

●● Enlace al texto completo (gratuito o de pago) 1016/j.bpg.2013.04.001

AUTORES / AUTHORS: - Zamboni G; Hirabayashi K; Castelli P; Lennon AM

INSTITUCIÓN / INSTITUTION: - Department of Pathology, University of Verona, Verona, Italy; Department of Pathology, Ospedale Sacro Cuore-Don Calabria, Via don Sempreboni, 5, Negrar, 37024 Verona, Italy. Electronic address: giuseppe.zamboni@sacrocuore.it.

RESUMEN / SUMMARY: - Pancreatic cancer has a very poor prognosis, with a five year survival of only 5%. New studies have shown that it takes over 11 years for cells to develop invasive capability. This provides an opportunity to intervene if precursor lesions can be detected. This paper reviews the molecular, pathological, clinical findings and management of pancreatic intraepithelial neoplasia (PanIN), intraductal pancreatic mucinous neoplasm (IPMN) and mucinous cystic neoplasm (MCN), three precursor lesions which can give rise to invasive carcinoma of the pancreas.

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[257]

TÍTULO / TITLE: - beta2-AR-HIF-1alpha: A Novel Regulatory Axis for Stress-Induced Pancreatic Tumor Growth and Angiogenesis.

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

REVISTA / JOURNAL: - Curr Mol Med. 2013 Jun 7;13(6):1023-34.

AUTORES / AUTHORS: - Shan T; Ma J; Ma Q; Guo K; Guo J; Li X; Li W; Liu J; Huang C; Wang F; Wu E

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary Surgery, First Affiliated Hospital of Medical College, Xi'an Jiaotong University, Xi'an 710061, Shaanxi, China. Erxi.Wu@ndsu.edu.

RESUMEN / SUMMARY: - The purpose of this study was to test the hypothesis that chronic stress in a negative social and psychological state plays a critical role in pancreatic cancer development and progression. In this study, we created a new stress model system to determine the effects of chronic stress on pancreatic cancer progression. Here, we show that chronic stress not only causes depression in mice, most likely attributed to an elevated level of epinephrine, but also induces pancreatic cancer progression. We provide evidence that the pancreatic cancer progression induced by chronic stress could be blocked to a significant degree by beta2-AR inhibitor ICI118 551 or HIF-1alpha inhibitor 2-methoxyestradiol. Moreover, establishment of pancreatic cancer in mice exposed to chronic stress was accompanied by up-regulation of the expression of MMP-2, MMP-9, and VEGF, mediated by a HIF- 1alpha-dependent beta-AR signaling pathway. Our data suggest that the beta2-AR-HIF-1alpha axis regulates stress-induced pancreatic tumor growth and angiogenesis. This study may have a therapeutic or preventive potential for the

patients with pancreatic cancer who are especially prone to psychosocial stress challenges.

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[258]

TÍTULO / TITLE: - Recent progress in pancreatic cancer.

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

REVISTA / JOURNAL: - CA Cancer J Clin. 2013 Jul 15. doi: 10.3322/caac.21190.

●● Enlace al texto completo (gratuito o de pago) 3322/caac.21190

AUTORES / AUTHORS: - Wolfgang CL; Herman JM; Laheru DA; Klein AP; Erdek MA; Fishman EK; Hruban RH

INSTITUCIÓN / INSTITUTION: - Associate Professor, Department of Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD; Associate Professor, Department of Oncology, The Sol Goldman Pancreatic Cancer Research Center, The Johns Hopkins University School of Medicine, Baltimore, MD; Associate Professor, Department of Pathology, The Sol Goldman Pancreatic Cancer Research Center, The Johns Hopkins University School of Medicine, Baltimore, MD.

RESUMEN / SUMMARY: - Answer questions and earn CME/CNE Pancreatic cancer is currently one of the deadliest of the solid malignancies. However, surgery to resect neoplasms of the pancreas is safer and less invasive than ever, novel drug combinations have been shown to improve survival, advances in radiation therapy have resulted in less toxicity, and enormous strides have been made in the understanding of the fundamental genetics of pancreatic cancer. These advances provide hope but they also increase the complexity of caring for patients. It is clear that multidisciplinary care that provides comprehensive and coordinated evaluation and treatment is the most effective way to manage patients with pancreatic cancer. CA Cancer J Clin 2013. Esta es una cita bibliográfica que va por delante de la publicación en papel. La fecha indicada en la cita provista, NO corresponde con la fecha o la cita bibliográfica de la publicación en papel. La cita bibliográfica definitiva (con el volumen y su paginación) saldrá en 1 ó 2 meses a partir de la fecha de la emisión electrónica-online. *** This is a bibliographic record ahead of the paper publication. The given date in the bibliographic record does not correspond to the date or the bibliographic citation on the paper publication. The publisher will provide the final bibliographic citation (with the volume, and pagination) within 1 or 2 months from the date the record was published online. © 2013 American Cancer Society.

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[259]

TÍTULO / TITLE: - An insulinoma presenting with hypochondriac delusions and food refusal.

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

REVISTA / JOURNAL: - Int Psychogeriatr. 2013 Jul 9:1-3.

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

1017/S104161021300104X

AUTORES / AUTHORS: - Renca S; Santos G; Cerejeira J

INSTITUCIÓN / INSTITUTION: - Centro Hospitalar e Universitario de Coimbra, EPE, Av. Bissaya Barreto - Praceta Prof. Mota Pinto, 3000-075 Coimbra, Portugal.

RESUMEN / SUMMARY: - ABSTRACT The authors report a case of a 68-year-old man with an unrecognized insulinoma manifesting with neuropsychiatric symptoms. For two years, he presented with unspecified behavior changes, autonomic and neuroglycopenic symptoms, which led him to be misdiagnosed with a neurologic and psychiatric disorder before the insulinoma was recognized. Following neurological alterations in context of hypoglycemia, subsequent to longstanding food refusal, he was admitted in the psychiatric ward. Despite good global response and normal food intake, hypoglycemic episodes were still occurring and led to a careful evaluation which permitted the definitive diagnostic. This case highlights the diagnostic difficulties of medical disorders presenting with clinical features overlapping neurological and psychiatric syndromes. It also reflects the diagnostic difficulties in rare clinical entities, particularly in patients previously followed in psychiatry and underlines the need for a constant dialogue and updating of clinicians.

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[260]

TÍTULO / TITLE: - Diagnostic and therapeutic role of endoscopy in gastroenteropancreatic neuroendocrine neoplasms.

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

REVISTA / JOURNAL: - Dig Liver Dis. 2013 May 31. pii: S1590-8658(13)00170-9. doi: 10.1016/j.dld.2013.04.007.

●● Enlace al texto completo (gratuito o de pago) 1016/j.dld.2013.04.007

AUTORES / AUTHORS: - Attili F; Capurso G; Vanella G; Fuccio L; Fave GD; Costamagna G; Larghi A

INSTITUCIÓN / INSTITUTION: - Digestive Endoscopy Unit, Catholic University, Rome, Italy.

RESUMEN / SUMMARY: - Gastroenteropancreatic neuroendocrine neoplasms have substantially increased over the last decades. Because of the indolent clinical course of the disease even in advance stages and the rise in the incidental diagnosis of small asymptomatic lesions, the prevalence of gastroenteropancreatic neuroendocrine neoplasms is higher than that of pancreatic, gastric and oesophageal adenocarcinomas, making them the second most prevalent cancer type of the gastrointestinal tract. This increase in the overall prevalence of gastroenteropancreatic neuroendocrine neoplasms has been paralleled by a growth in the importance of the endoscopist in the care of these patients, who usually require a multidisciplinary approach. In this

manuscript the diagnostic and therapeutic role of endoscopic for gastroenteropancreatic neuroendocrine neoplasms will be reviewed.

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[261]

TÍTULO / TITLE: - Pancreatic cancer in Saudi patients treated at tertiary institution. Ten years retrospective study.

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

REVISTA / JOURNAL: - Saudi Med J. 2013 Jun;34(6):604-8.

AUTORES / AUTHORS: - AlGhamdi HJ; Alfaifi SA; Alolayan AA; Musaad SM; Jazieh AM

INSTITUCIÓN / INSTITUTION: - Oncology Department, King Abdulaziz Medical City, Riyadh, Kingdom of Saudi Arabia.

RESUMEN / SUMMARY: - OBJECTIVES: To describe presentation, management, and outcome, and determine prognostic factors for pancreatic cancer patients. METHODS: A retrospective review of patients diagnosed with pancreatic cancer at King Abdulaziz Medical City, Riyadh, Saudi Arabia during the period from January 2000 to December 2010. Descriptive statistics were conducted on the collected data and survival was estimated using the Kaplan Meier estimate. Univariate and multiple regression analyses were carried out. RESULTS: The medical records of 179 patients were reviewed. The patients' median age was 63 years ranging from 15-96 years, and 116 (64.8%) of them were male. The one-year survival rate was 39% and the 5-year survival was 10%. The median overall survival (OS) was 6.9 months. Age at diagnosis, grade, T stage, N stage, M stage, TNM stage group, and the combined stage group (stage III/IV versus others), site of distant metastasis, carcinoembryonic antigen (CEA), carbohydrate antigen 19-9, surgery and chemotherapy were significant predictors for OS on an univariate Cox proportional hazards regression analysis. A multiple regression model including all the significant predictors was conducted. Age at the time of diagnosis and M stage were significant variables. CONCLUSION: Our patients present at a younger age and have better 5-year survival compared with the United States Surveillance Epidemiology and End Results data, which deserves further evaluation. Age and disease stage were identified as independent prognostic factors for survival in this patient population.

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[262]

TÍTULO / TITLE: - Pancreatic cancer: advances in treatment, results and limitations.

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

REVISTA / JOURNAL: - Dig Dis. 2013;31(1):51-6. doi: 10.1159/000347178. Epub 2013 Jun 17.

●● Enlace al texto completo (gratuito o de pago) 1159/000347178

AUTORES / AUTHORS: - Hackert T; Buchler MW
INSTITUCIÓN / INSTITUTION: - Department of General, Visceral and Transplantation Surgery, University of Heidelberg, Heidelberg, Germany.
RESUMEN / SUMMARY: - Background/Aims: Pancreatic cancer remains a therapeutic challenge. Surgery is the only treatment with the chance of cure. The aim of this review is to summarize the present state-of-the-art surgical procedures in pancreatic cancer. Methods: The current literature was reviewed with regard to surgical approaches in pancreatic cancer. A focus was put on high-quality studies, reviews, systematic reviews and meta-analyses as well as recruiting studies highlighting innovative approaches. Results: Today, standard resections can be performed with mortality rates below 5% in specialized high-volume institutions. Extended approaches for locally advanced cancer are technically feasible, including venous resections, multivisceral resections and recurrence surgery. They can be carried out without increased morbidity and mortality, are not compromised by higher R1 or N+ rates, and can improve survival. Arterial tumor invasion is still regarded controversially and is oncologically questionable. All surgical approaches should be part of interdisciplinary multimodal treatment concepts to improve the patients' prognosis. Conclusion: Surgery is the backbone of pancreatic cancer treatment in localized disease. Extended approaches are feasible in centers and show - except for arterial resections - good long-term outcome. Interdisciplinary therapy is an essential supplementation of all surgical approaches.

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[263]
TÍTULO / TITLE: - Value of carbohydrate antigen 19-9 in predicting response and therapy control in patients with metastatic pancreatic cancer undergoing first-line therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Front Oncol. 2013 Jun 14;3:155. doi: 10.3389/fonc.2013.00155. Print 2013.
●● Enlace al texto completo (gratuito o de pago) 3389/fonc.2013.00155
AUTORES / AUTHORS: - Pelzer U; Hilbig A; Sinn M; Stieler J; Bahra M; Dorken B; Riess H
INSTITUCIÓN / INSTITUTION: - Department of Hematology/Oncology, Comprehensive Cancer Center, Universitatsmedizin Berlin - Charite , Berlin , Germany.
RESUMEN / SUMMARY: - Background: Serum carbohydrate antigen 19-9 (CA 19-9) has been shown to be a sensitive and specific serum marker for pancreatic cancer. Little has been published about correlations between baseline CA 19-9 level or changes to CA 19-9 level and median overall survival (mOS). Its impact on monitoring treatment efficacy remains under discussion, however. Methods: CA 19-9 serum level was measured in 181 consecutive patients with advanced pancreatic cancer (APC) being treated with gemcitabine-based first-line

chemotherapy. We separated the patients into several groups depending on baseline CA 19-9 levels and the CA 19-9 response after 6-8 weeks of treatment. Evaluations were made using SPSS 19.9. Results: Median baseline CA 19-9 level was 1,493 U/ml (range 40-1,043,301). Patients with baseline CA 19-9 </=1,000 U/ml had a mOS of 14.9 months (95% CI: 11.36:18.44), whereas patients with CA 19-9>1,000 U/ml had a mOS of 7.4 months [(95% CI: 5.93:8.87) p < 0.001, HR 2.12]. With regard to the change in CA 19-9 after 6-8 weeks of treatment: patients with increased CA 19-9 levels had a mOS of 8.1 months, those with stabilized CA 19-9 levels 11.6 months, and those with decreased CA 19-9 levels 11.1 months (p < 0.019). Conclusion: CA 19-9 levels can separate patients with differing mortality risks at baseline. Patients with stabilization or high response of CA 19-9 after 6-8 weeks of treatment had no significant differences in survival rates, whereas patients with increased CA 19-9 had significantly lower survival rates, indicating an early treatment failure.

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[264]

TÍTULO / TITLE: - Effect of Jinlong capsule on proliferation and apoptosis of human pancreatic cancer cells BxPC-3.

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

REVISTA / JOURNAL: - J Tradit Chin Med. 2013 Apr;33(2):205-10.

AUTORES / AUTHORS: - Li Y; Hu J; Huang H; He Y

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Guang'an men Hospital Affiliated to China Academy of Chinese Medical Sciences, Beijing 100053, China.

RESUMEN / SUMMARY: - OBJECTIVE: To study the possible roles of Jinlong capsule (JLC) on the proliferation and apoptosis of human pancreatic cancer cells BxPC-3. METHODS: The human pancreatic cancer cells BxPC-3 were treated with JLC at the concentration of 0.05-1.00 mg/mL for 24-120 h. The inhibition rate of JLC on human pancreatic cancer cells BxPC-3 was detected by 3-(4,5-dimethiylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay. Flow cytometry was employed to measure cell apoptosis using Annexin V-FITC/Propidium iodide (AV-FITC/PI) method. Cell cycles were determined by PI staining. The expression of 5100 Calcium binding protein A4 (S100A4) in cell matrix was measured by enzyme-linked immunosorbent assay (ELISA). The expression levels of apoptosis-related protein such as BCL2/adenovirus E1B 19 kDa interacting protein 3 (BNIP3), B-cell lymphoma/leukemia-2 (Bcl-2) and Cys-teinylaspartate specific proteinase 3 (Caspase-3) were detected by Western blotting. RESULTS: JLC significantly inhibited the proliferation of human pancreatic cancer cells BxPC-3 in a dose-dependent and time-dependent manner. JLC promoted cell apoptosis and maintained cell cycle in S and G2/M phase rather than G1/G0 phase. The expression of 5100ª4 in the cell matrix was reduced. The expression of cell apoptotic protein BNIP3 was increased while Bcl-2 was decreased. CONCLUSION: JLC can inhibit the proliferation of human pancreatic cancer cells BxPC-3 by stimulating cell apoptosis, arresting

the cell cycle at S and G2/M phase which blocks the circulation of normal cell cycle and reducing the expression of S100A4 protein. Higher pro-apoptosis protein BNIP3 and lower anti-apoptosis protein Bcl-2 levels were found, which may be related to the apoptotic effects of JLC.

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[265]

TÍTULO / TITLE: - Preoperative diagnosis of a solid pseudopapillary tumour of the pancreas by Endoscopic Ultrasound Fine Needle Biopsy: A retrospective case series.

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

REVISTA / JOURNAL: - Dig Liver Dis. 2013 Jul 19. pii: S1590-8658(13)00219-3. doi: 10.1016/j.dld.2013.06.005.

●● Enlace al texto completo (gratuito o de pago) 1016/j.dld.2013.06.005

AUTORES / AUTHORS: - Maimone A; Luigiano C; Baccarini P; Fornelli A; Cennamo V; Polifemo A; Fiscaletti M; de Biase D; Jaboli F; Virgilio C; Stelitano L; Zanini N; Masetti M; Jovine E; Fabbri C

INSTITUCIÓN / INSTITUTION: - Unit of Gastroenterology, AUSL Bologna Bellaria-Maggiore Hospital, Bologna, Italy.

RESUMEN / SUMMARY: - BACKGROUND: A solid pseudopapillary tumour of the pancreas (SPTP) is a rare neoplasm. AIM: We herein present five cases of SPTP diagnosed using endoscopic ultrasound (EUS) guided fine-needle biopsy (FNB) using a needle with side fenestration (ProCore-needle). METHODS: From January 2011 to June 2012 in five patients with SPTP tissue acquisition was carried out with a 19-gauge (4 patients) or a 22-gauge (one patient) needle. RESULTS: The mean age of the patients was 30.8 years, the mean lesion size was 49mm and the most common location was the tail of the pancreas (3 cases). When the samples were evaluated macroscopically, small core fragments were observed in all cases. A preoperative diagnosis of SPTP was made in all patients on the basis of the histocytological and characteristic immunophenotypic patterns and was confirmed at final surgical histology. CONCLUSIONS: In our experience, EUS-FNB is an effective and secure method for a preoperative diagnosis of SPTP.

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[266]

TÍTULO / TITLE: - Targeting cathepsin e in pancreatic cancer by a small molecule allows in vivo detection.

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

REVISTA / JOURNAL: - Neoplasia. 2013 Jul;15(7):684-93.

AUTORES / AUTHORS: - Keliher EJ; Reiner T; Earley S; Klubnick J; Tassa C; Lee AJ; Ramaswamy S; Bardeesy N; Hanahan D; Depinho RA; Castro CM; Weissleder R

INSTITUCIÓN / INSTITUTION: - Center for Systems Biology, Massachusetts General Hospital, Boston, MA.
RESUMEN / SUMMARY: - When resectable, invasive pancreatic ductal adenocarcinoma (PDAC) is most commonly treated with surgery and radiochemotherapy. Given the intricate local anatomy and locoregional mode of dissemination, achieving clean surgical margins can be a significant challenge. On the basis of observations that cathepsin E (CTSE) is overexpressed in PDAC and that an United States Food and Drug Administration (FDA)-approved protease inhibitor has high affinity for CTSE, we have developed a CTSE optical imaging agent [ritonavir tetramethyl-BODIPY (RIT-TMB)] for potential intraoperative use. We show nanomolar affinity [half maximal inhibitory concentration (IC50) of 39.9 +/- 1.2 nM] against CTSE of the RIT-TMB in biochemical assays and intracellular accumulation and target-to-background ratios that allow specific delineation of individual cancer cells. This approach should be useful for more refined surgical staging, planning, and resection with curative intent.

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[267]
TÍTULO / TITLE: - Pancreatic cancer stem cells: their role in pancreatic cancer patient outcomes and what is future?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):401-4. doi: 10.6092/1590-8577/1658.
AUTORES / AUTHORS: - Habib M; Saif MW
INSTITUCIÓN / INSTITUTION: - Steward St. Elizabeth Medical Center, Tufts University School of Medicine. Boston, MA, USA. dmhabib@gmail.com.
RESUMEN / SUMMARY: - There is emerging evidence that stem cells might be playing an important role when it comes to cancer aggressiveness, metastasis, recurrence, resistance to chemotherapy and overall survival in hematologic malignancies as well as solid tumors including pancreatic adenocarcinoma. We review Abstract #e15058 presented at the 2013 ASCO Annual Meeting in Chicago by Andrikou et al. Pancreatic cancer patients over-expressing pancreatic cancer stem cell markers were associated with aggressive tumors and worse survival.

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[268]
TÍTULO / TITLE: - Intraductal tubulopapillary neoplasms of the pancreas: case report and review of the literature.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Nippon Med Sch. 2013;80(3):224-9.
AUTORES / AUTHORS: - Kasugai H; Tajiri T; Takehara Y; Mukai S; Tanaka J; Kudo SE

INSTITUCIÓN / INSTITUTION: - Digestive Disease Center, Showa University Northern Yokohama Hospital.
RESUMEN / SUMMARY: - A 69-year-old woman was referred to our hospital after incidental identification of a pancreatic mass during follow-up for diabetes mellitus. Various imaging examinations showed a tumor in the main pancreatic duct, without apparent hypersecretion of mucin. Brush cytologic examination revealed class V disease (adenocarcinoma). Because preoperative examination suggested an intraductal neoplasm with associated invasive cancer, total pancreatectomy was performed. Histological examination, based on current World Health Organization classifications, suggested a diagnosis of intraductal tubulopapillary neoplasm. A small cystic lesion adjacent to the intraductal tubulopapillary neoplasm was incidentally diagnosed as serous cystadenoma. The patient has remained well without recurrence as of 24 months postoperatively. Computed tomography and magnetic resonance imaging of the intraductal tubulopapillary neoplasm suggested ductal cell carcinoma of the pancreas rather than intraductal papillary mucinous neoplasm. Distinguishing intraductal tubulopapillary neoplasm from ductal cell carcinoma is clinically important, as intraductal tubulopapillary neoplasm has a favorable prognosis after curative resection.

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[269]
TÍTULO / TITLE: - Solid pseudopapillary tumor of the pancreas: A case series of 9 patients.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Turk J Gastroenterol. 2012 Dec;23(6):727-35.
AUTORES / AUTHORS: - Ozkara S; Aker FV; Yitik A; Tosun I; Saethla A; Cetinkaya ZA; Gumrukcu G; Tisgaoethlu N
INSTITUCIÓN / INSTITUTION: - HaydarpaSa Numune Education and Research Hospital, Department of Pathology, istanbul, E-Mail: selvinazo@gmail.com.
RESUMEN / SUMMARY: - Background/aims:Solid pseudopapillary tumor is a rare exocrine tumor of the pancreas. There is no clear consensus on its etiology, origin and treatment. In this study, the clinical, pathological and immunohistochemical features of nine patients with solid pseudopapillary tumor were re-evaluated in view of the current literature findings. Materials and Methods: We studied nine cases diagnosed with solid pseudopapillary tumor between 2005 and 2010. The clinical, pathological and laboratory data were analyzed. Results: On microscopy, all tumors had well-defined borders and were separated from surrounding pancreatic tissue by a thick fibrous capsule. The tumor consisted mainly of pseudopapillary structures with focal solid areas accompanied by wide hemorrhagic and cystic regions. The typical morphological features were present to varying degrees. Of the nine cases, one relapsed approximately two years after the diagnosis, and our laboratory also evaluated the surgical specimen of local recurrence. Conclusions: While some

new light has been shed on the clinicopathological features of solid pseudopapillary tumor concerning its etiology, origin and treatment methods, there is much to be understood. Further studies focusing on genetics, pathogenesis and prognosis are needed for a better understanding of this entity.

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[270]

TÍTULO / TITLE: - Role of resection of the primary pancreatic neuroendocrine tumor in the multidisciplinary treatment of patients with unresectable synchronous liver metastases: a case series.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):415-22. doi: 10.6092/1590-8577/1291.

AUTORES / AUTHORS: - Kondo NI; Ikeda Y; Maehara S; Sugimoto R; Nishiyama K; Sakaguchi Y

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery, National Hospital Organization Kyushu Cancer Center. Fukuoka City, Japan. kondo-n@surg2.med.kyushu-u.ac.jp.

RESUMEN / SUMMARY: - CONTEXT: Liver metastases have often existed in patients who have pancreatic neuroendocrine tumors (pNETs) at the time of diagnosis. In the management of patients of pNETs with unresectable liver metastases, the clinical efficacy of surgery to primary pancreatic tumor has been controversial. We presented four patients who were treated with resection of primary pancreatic tumor, trans-arterial hepatic treatment and systemic therapies. We reviewed literatures and discussed about role of resection of primary pancreatic tumor in the multidisciplinary treatment. METHODS: We retrieved medical records of patients who had been histopathologically diagnosed as pNETs at our institution between April 2000 and March 2006, and found 4 patients who had pNETs with unresectable synchronous liver metastases and no extrahepatic metastases. All patients received resection of primary tumor. Patients' demographics, pathology, treatment, short- and long-term outcome were examined. RESULTS: In short-term outcome analysis, delayed gastric emptying was developed in one patient who received pancreaticoduodenectomy. There were no other significant postoperative complications. As for long-term outcome, two patients who received distal pancreatectomy, sequential trans-arterial treatments and systemic therapies could survive for long time relatively. They died 92 and 73 months after the first treatment, respectively. One patient who received distal pancreatectomy and trans-arterial treatment died from unrelated disease 14 months after the first treatment. Another patient who received preoperative trans-arterial treatments and pancreaticoduodenectomy rejected postoperative trans-arterial treatment, was treated with systemic therapies and died 37 months after the initial treatment. CONCLUSIONS: Resection of primary pNETs would be considered

as an optional treatment for the selected patients who had unresectable synchronous liver metastases in the process of the multidisciplinary approach.

TÍTULO / TITLE: - A proteomic comparison of formalin-fixed paraffin-embedded pancreatic tissue from autoimmune pancreatitis, chronic pancreatitis, and pancreatic cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):405-14. doi: 10.6092/1590-8577/1508.

AUTORES / AUTHORS: - Paulo JA; Kadiyala V; Brizard S; Banks PA; Steen H; Conwell DL

INSTITUCIÓN / INSTITUTION: - Center for Pancreatic Disease, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital and Department of Medicine, Harvard Medical School. Boston, MA, USA. dconwell@partners.org.

RESUMEN / SUMMARY: - CONTEXT: Formalin-fixed paraffin-embedded (FFPE) tissue is a standard for specimen preservation, and as such FFPE tissue banks are an untapped resource of histologically-characterized specimens for retrospective biomarker investigation for pancreatic disease. OBJECTIVES: We use liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) to compare FFPE specimens from three different diseases of the exocrine pancreas. DESIGN: We investigated the proteomic profile of FFPE pancreatic tissue from 9 archived specimens that were histologically classified as: autoimmune pancreatitis (n=3), chronic pancreatitis (n=3), and pancreatic cancer (n=3), using LC-MS/MS. SETTING: This is a proteomic analysis experiment of FFPE pancreatic tissue in an academic center. PATIENTS: FFPE tissue specimens were provided by Dana-Farber/Harvard Cancer Center (Boston, MA, USA). INTERVENTIONS: FFPE tissue specimens were collected via routine surgical resection procedures. MAIN OUTCOME MEASURES: We compared proteins identified from chronic pancreatitis, autoimmune pancreatitis, and pancreatic cancer FFPE pancreatic tissue. RESULTS: We identified 386 non-redundant proteins from 9 specimens. Following our filtering criteria, 73, 29, and 53 proteins were identified exclusively in autoimmune pancreatitis, chronic pancreatitis, and pancreatic cancer specimens, respectively. CONCLUSIONS: We report that differentially-expressed proteins can be identified among FFPE tissues specimens originating from individuals with different histological diagnoses. These proteins merit further confirmation with a greater number of specimens and orthogonal validation, such as immunohistochemistry. The mass spectrometry-based methodology used herein has the potential to enhance diagnostic biomarker and therapeutic target discovery, further advancing pancreatic research.

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[271]

TÍTULO / TITLE: - Pancreas serous cystadenoma: typical imaging aspect of a rare tumor.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JBR-BTR. 2013 Mar-Apr;96(2):89.
AUTORES / AUTHORS: - Kirchgesner T; Sleiman WB; Hamoir X; Salovic D; Kirsch J
INSTITUCIÓN / INSTITUTION: - CHWAPI, Site Notre Dame, Service de radiologie, Avenue Delmee 9, 7500 Tournai, Belgium.

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[272]
TÍTULO / TITLE: - Laparoscopic distal pancreatectomy preserving the spleen and splenic vessels for benign and low-grade malignant pancreatic neoplasm.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Fukuoka Igaku Zasshi. 2013 Mar;104(3):54-63.
AUTORES / AUTHORS: - Ikeda T; Yoshiya S; Toshima T; Harimoto N; Yamashita Y; Ikegami T; Yoshizumi T; Soejima Y; Shirabe K; Maehara Y
INSTITUCIÓN / INSTITUTION: - Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan. t-ikeda@surg2.med.kyushu-u.ac.jp
RESUMEN / SUMMARY: - BACKGROUND/AIMS: Laparoscopic spleen-preserving distal pancreatectomy (LSPDP) is expected to be less invasive than laparoscopic distal pancreatectomy with splenectomy. However, there are few reports regarding the details of the procedure for LSPDP, and its safety remains unclear. This study aimed to evaluate the feasibility and safety of LSPDP. METHODOLOGY: Six patients underwent LSPDP from March 2009 to February 2013 in our center, and their clinical data and outcomes were reviewed retrospectively. RESULTS: A total of six laparoscopic distal pancreatic resections were attempted in four female and two male patients. All of the operations were successful, with an average operative time of 290.7 min (range: 211-377 min) and an average blood loss of 43.5 g (range: 0-142 g). The mean hospital stay was 11.8 days (range: 9-17days). No obvious pancreatic fistulas occurred, although pseudocysts at the stump of the pancreas were recognized in three patients on CT scans performed at 7 days postoperatively. Postoperative pathological examinations revealed two cases of serous cystadenoma in the body and tail of the pancreas, one case of serous oligocystic adenoma, one case of mucinous cystadenoma, one case of neuroendocrine tumor, and one case of solid-pseudopapillary neoplasm. CONCLUSIONS: LSPDP is minimally invasive, safe, and feasible for the management of benign pancreatic tail tumors, with the advantages of earlier recovery and less morbidity from complications.

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[273]

TÍTULO / TITLE: - Juzentaihoto Failed to Augment Antigen-Specific Immunity but Prevented Deterioration of Patients' Conditions in Advanced Pancreatic Cancer under Personalized Peptide Vaccine.

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

REVISTA / JOURNAL: - Evid Based Complement Alternat Med. 2013;2013:981717. doi: 10.1155/2013/981717. Epub 2013 Jun 10.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/981717

AUTORES / AUTHORS: - Yutani S; Komatsu N; Matsueda S; Yoshitomi M; Shirahama T; Yamada A; Itoh K; Sasada T

INSTITUCIÓN / INSTITUTION: - Department of Immunology and Immunotherapy, Kurume University School of Medicine, Kurume 830-0011, Japan.

RESUMEN / SUMMARY: - Juzentaihoto (JTT) is a well-known Japanese herbal medicine, which has been reported to modulate immune responses and enhance antitumor immunity in animal models. However, it is not clear whether JTT has similar effects on humans. In particular, there is little information on the effects of JTT in antigen-specific immunity in cancer patients. Here we conducted a randomized clinical study to investigate whether combined usage of JTT could affect antigen-specific immunity and clinical findings in advanced pancreatic cancer patients undergoing personalized peptide vaccination (PPV), in which HLA-matched vaccine antigens were selected based on the preexisting host immunity. Fifty-seven patients were randomly assigned to receive PPV with (n = 28) or without (n = 29) JTT. Unexpectedly, JTT did not significantly affect cellular or humoral immune responses specific to the vaccine antigens, which were determined by antigen-specific interferon-gamma secretion in T cells and antigen-specific IgG titers in plasma, respectively. Nevertheless, JTT prevented deterioration of patients' conditions, such as anemia, lymphopenia, hypoalbuminemia, plasma IL-6 elevation, and reduction of performance status, which are frequently observed in advanced cancers. To our knowledge, this is the first clinical study that examined the immunological and clinical effects of JTT in cancer patients undergoing immunotherapy in humans.

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[274]

TÍTULO / TITLE: - Diagnostic and Prognostic Impact of Circulating YKL-40, IL-6, and CA 19.9 in Patients with Pancreatic Cancer.

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

REVISTA / JOURNAL: - PLoS One. 2013 Jun 26;8(6):e67059. Print 2013.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0067059

AUTORES / AUTHORS: - Schultz NA; Christensen IJ; Werner J; Giese N; Jensen BV; Larsen O; Bjerregaard JK; Pfeiffer P; Calatayud D; Nielsen SE; Yilmaz MK; Hollander NH; Wojdemann M; Bojesen SE; Nielsen KR; Johansen JS

INSTITUCIÓN / INSTITUTION: - Department of Surgical Gastroenterology and Transplantation, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark ; Department of Oncology Copenhagen University Hospital at Herlev,

Denmark ; Department of Surgical Gastroenterology, Copenhagen University Hospital at Herlev, Herlev, Denmark ; Department of Medicine, Copenhagen University Hospital at Herlev, Herlev, Denmark.

RESUMEN / SUMMARY: - PURPOSE: We tested the hypothesis that high plasma YKL-40 and IL-6 associate with pancreatic cancer and short overall survival. PATIENTS AND METHODS: In all, 559 patients with pancreatic cancer from prospective biomarker studies from Denmark (n = 448) and Germany (n = 111) were studied. Plasma YKL-40 and IL-6 were determined by ELISAs and serum CA 19.9 by chemiluminescent immunometric assay. RESULTS: Odds ratios (ORs) for prediction of pancreatic cancer were significant for all biomarkers, with CA 19.9 having the highest AUC (CA 19.9: OR = 2.28, 95% CI 1.97 to 2.68, p<0.0001, AUC = 0.94; YKL-40: OR = 4.50, 3.99 to 5.08, p<0.0001, AUC = 0.87; IL-6: OR = 3.68, 3.08 to 4.44, p<0.0001, AUC = 0.87). Multivariate Cox analysis (YKL-40, IL-6, CA 19.9, age, stage, gender) in patients operated on showed that high preoperative IL-6 and CA 19.9 (dichotomized according to normal values) were independently associated with short overall survival (CA 19.9: HR = 2.51, 1.22-5.15, p = 0.013; IL-6: HR = 2.03, 1.11 to 3.70, p = 0.021). Multivariate Cox analysis of non-operable patients (Stage IIB-IV) showed that high pre-treatment levels of each biomarker were independently associated with short overall survival (YKL-40: HR = 1.30, 1.03 to 1.64, p = 0.029; IL-6: HR = 1.71, 1.33 to 2.20, p<0.0001; CA 19.9: HR = 1.54, 1.06 to 2.24, p = 0.022). Patients with preoperative elevation of both IL-6 and CA 19.9 had shorter overall survival (p<0.005) compared to patients with normal levels of both biomarkers (45% vs. 92% alive after 12 months). CONCLUSIONS: Plasma YKL-40 and IL-6 had less diagnostic impact than CA 19.9. Combination of pretreatment YKL-40, IL-6, and CA 19.9 may have clinical value to identify pancreatic cancer patients with the poorest prognosis.

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[275]

TÍTULO / TITLE: - Genetic variants in vitamin d pathway genes and risk of pancreas cancer; results from a population-based case-control study in ontario, Canada.

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

REVISTA / JOURNAL: - PLoS One. 2013 Jun 24;8(6):e66768. doi: 10.1371/journal.pone.0066768. Print 2013.

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

1371/journal.pone.0066768

AUTORES / AUTHORS: - Anderson LN; Cotterchio M; Knight JA; Borgida A; Gallinger S; Cleary SP

INSTITUCIÓN / INSTITUTION: - Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario, Canada.

RESUMEN / SUMMARY: - Recent studies of 25-hydroxyvitamin D (25(OH)D) levels and pancreas cancer have suggested a potential role of the vitamin D pathway in the etiology of this fatal disease. Variants in vitamin-D related genes

are known to affect 25(OH)D levels and function and it is unknown if these variants may influence pancreatic cancer risk. The association between 87 single nucleotide polymorphisms (SNPs) in 11 genes was evaluated within the Ontario Pancreas Cancer Study, a population-based case-control study. Pancreatic cancer cases with pathology confirmed adenocarcinoma were identified from the Ontario Cancer Registry (n = 628) and controls were identified through random digit dialing (n = 1193). Age and sex adjusted odds ratios (OR) and 95% confidence intervals (CI) were estimated by multivariate logistic regression. SNPs in the CYP24A1, CYP2R1, calcium sensing receptor (CASR), vitamin D binding protein (GC), retinoid X receptor-alpha (RXRA) and megalin (LRP2) genes were significantly associated with pancreas cancer risk. For example, pancreas cancer risk was inversely associated with CYP2R1 rs10741657 (AA versus GG, OR = 0.70; 95%CI: 0.51-0.95) and positively with CYP24A1 rs6127119 (TT versus CC. OR = 1.94; 95%CI: 1.28-2.94). None of the associations were statistically significant after adjustment for multiple comparisons. Vitamin D pathway gene variants may be associated with pancreas cancer risk and future studies are needed to understand the possible role of vitamin D in tumorigenesis and may have implications for cancer-prevention strategies.

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[276]

TÍTULO / TITLE: - Comment on: Risk of Pancreatic Cancer in Relation to ABO Blood Group and Hepatitis C Virus Infection in Korea: A Case-Control Study.

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

REVISTA / JOURNAL: - J Korean Med Sci. 2013 Jul;28(7):1114-5. doi: 10.3346/jkms.2013.28.7.1114.

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

3346/jkms.2013.28.7.1114

AUTORES / AUTHORS: - Kabir A

INSTITUCIÓN / INSTITUTION: - Candidate of Epidemiology, Department of Epidemiology; Faculty of Public Health; Shahid Beheshti University of Medical Sciences, and Center for Educational Research in Medical Sciences; Tehran University of Medical Sciences, Tehran, Iran.

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[277]

TÍTULO / TITLE: - Multimodal Treatment Eliminates Cancer Stem Cells and Leads to Long-Term Survival in Primary Human Pancreatic Cancer Tissue Xenografts.

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

REVISTA / JOURNAL: - PLoS One. 2013 Jun 18;8(6):e66371. Print 2013.

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

1371/journal.pone.0066371

AUTORES / AUTHORS: - Hermann PC; Trabulo SM; Sainz B Jr; Balic A; Garcia E; Hahn SA; Vandana M; Sahoo SK; Tunici P; Bakker A; Hidalgo M; Heeschen C
INSTITUCIÓN / INSTITUTION: - Stem Cells and Cancer Group, Clinical Research Programme, Spanish National Cancer Research Centre (CNIO), Madrid, España.
RESUMEN / SUMMARY: - PURPOSE: In spite of intense research efforts, pancreatic ductal adenocarcinoma remains one of the most deadly malignancies in the world. We and others have previously identified a subpopulation of pancreatic cancer stem cells within the tumor as a critical therapeutic target and additionally shown that the tumor stroma represents not only a restrictive barrier for successful drug delivery, but also serves as a paracrine niche for cancer stem cells. Therefore, we embarked on a large-scale investigation on the effects of combining chemotherapy, hedgehog pathway inhibition, and mTOR inhibition in a preclinical mouse model of pancreatic cancer. EXPERIMENTAL DESIGN: Prospective and randomized testing in a set of almost 200 subcutaneous and orthotopic implanted whole-tissue primary human tumor xenografts. RESULTS: The combined targeting of highly chemoresistant cancer stem cells as well as their more differentiated progenies, together with abrogation of the tumor microenvironment by targeting the stroma and enhancing tissue penetration of the chemotherapeutic agent translated into significantly prolonged survival in preclinical models of human pancreatic cancer. Most pronounced therapeutic effects were observed in gemcitabine-resistant patient-derived tumors. Intriguingly, the proposed triple therapy approach could be further enhanced by using a PEGylated formulation of gemcitabine, which significantly increased its bioavailability and tissue penetration, resulting in a further improved overall outcome. CONCLUSIONS: This multimodal therapeutic strategy should be further explored in the clinical setting as its success may eventually improve the poor prognosis of patients with pancreatic ductal adenocarcinoma.

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[278]
TÍTULO / TITLE: - Locally advanced pseudopapillary neoplasm of the pancreas in a male patient: a case report.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):438-41. doi: 10.6092/1590-8577/1363.
AUTORES / AUTHORS: - Attaallah W; Javadov M; Ayranci FG; Filinte D; Dulundu E; Yegen C
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Marmara University School of Medicine. Istanbul, Turkey. drwafi2003@yahoo.com.
RESUMEN / SUMMARY: - CONTEXT: Solid pseudopapillary tumor of the pancreas is a rare neoplasm, predominantly observed in young women and with greatest incidence in the second and third decade. Although large at the time of diagnosis, it has clinically good behavior. The occurrence of infiltrating varieties

of solid pseudopapillary tumors is very rare. CASE REPORT: We report the case of a 48-year-old man with a giant mass in the pancreas, incidentally discovered during an abdominal ultrasonography. The mass was later investigated using multidetector computed tomography and magnetic resonance imaging. The lobulated lesion had cystic-necrotic appearances which lead the radiologists to suggest the possibility of either a gastrointestinal stromal tumor or a pancreatic cancer. The patient was operated. Operative signs showed that the tumor invaded the splenic hilum and mesentery of transverse colon. En-block resection of pancreas, spleen and transverse colon was performed as the mass was thought to be a locally advanced pancreas tumor. Pathological diagnosis reported a solid pseudopapillary tumor. CONCLUSION: Although solid pseudopapillary tumor is considered a rare tumor, with a very rare rate of locally infiltrating variety, and rarely presents in males, it must be kept in mind while making the differential diagnosis of cystic pancreatic lesions to begin appropriate clinical management.

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[279]

TÍTULO / TITLE: - Serum hepatitis a antibody positivity correlates with higher pancreas cancer mortality in adults: implications for hepatitis vaccination in high risk areas.

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

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(5):2707-10.

AUTORES / AUTHORS: - Cheung MR

INSTITUCIÓN / INSTITUTION: - 275 S Bryn Mawr Ave, K43, Bryn Mawr, PA, USA E-mail : cheung.r100@gmail.com.

RESUMEN / SUMMARY: - Background: This study used pre-hepatitis A vaccination era data in U.S. to study the relationship between serum hepatitis A antibody positivity with pancreas cancer mortality in adults. Patients and Methods: Public use National Health and Nutrition Examination Survey (NHANES III) data were employed. NHANES III uses complex probabilistic methods to sample nationally representative samples. Household adult laboratory and mortality data were merged. Sample persons who were available to be examined in the Mobile Examination Center (MEC) were included in this study. All results were obtained by using specialized survey software taking into account the primary sampling unit and stratification variables and the weights assigned to the sample persons examined in the MEC. Thus they are representative of the U.S. population. Results: The mean risk (95%CI) of death in the study population for pancreas cancer was 0.0014 (-0.000069 -.0029); their mean age (95%CI) at the mobile examination center (MXPAXTMR) was 473.43 (463.85-482.10); the follow up in months from their medical examination (permth_exm) was 170.12 (164.17-176.07). The odds ratios (S.E.) of the statistically significant univariables were: age, 1.007 (1.005-1.009); serum anti-hepatitis antibody status, 0.038 (0.004-0.376); and drinking hard liquor, 1.014 (1.004-1.023). The coefficients (S.E.) of the statistically significant variables

after multivariate analysis were 0.006 (0.002-0.010) for age and -2.528 (-4.945--0.111) for serum anti-hepatitis A antibody negativity (using serum anti-hepatitis A antibody positivity as a reference). Conclusion: Serum hepatitis A antibody positivity correlates with higher pancreas cancer mortality in adults.

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[280]

TÍTULO / TITLE: - Endobiliary Stent: Marker for Patient Alignment in Image-Guided Radiotherapy in Pancreatic and Periampullary Cancers.

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

REVISTA / JOURNAL: - J Gastrointest Cancer. 2013 Jun 4.

●● Enlace al texto completo (gratuito o de pago) 1007/s12029-013-9508-4

AUTORES / AUTHORS: - Shukla P; Engineer R; Chopra S; Shrivastava SK

INSTITUCIÓN / INSTITUTION: - Departments of Radiation Oncology and Medical Physics, Tata Memorial Hospital, Tata Memorial Centre, Parel, Mumbai, 400012, India.

RESUMEN / SUMMARY: - PURPOSE: The aim of this study was to analyse the possibility of using stent in pretreatment megavoltage computed tomography (MVCT) images with respect to that on planning kilovoltage computed tomography as tumour surrogate during matching for daily registration in cases of pancreatic and periampullary cancer treated on a TomoTherapy Hi-Art system. METHODS: Planning CT and pretreatment MVCT of the first and then after every three fractions were transferred to a FocalSim workstation for ten patients. Planning CT of each patient was independently fused with each of the seven MVCT images of that patient. The stent was contoured on all of the eight images for each patient. The difference between the three co-ordinates of centre of mass (CM) of the stent on the planning CT and seven MVCT images was found. The difference between CM of the liver and stents on the planning CT as well as on the MVCT for all seven fractions was also calculated. The mean of these differences across all patients was calculated and analysed. RESULTS: The mean difference in planning and MVCT CMs for stents in the X, Y and Z directions was 0.13 cm (+/-0.4), 0.16 cm (+/-2.2) and 0.35 cm (+/-0.7), respectively. Average difference between CM of the liver and stent on the planning CT in the X, Y and Z directions was found to be 1.832 cm (+/-1.64), 5.34 cm (+/-1.33) and 0.54 cm (+/-0.26), respectively. Average difference between CM of the liver and CM of stent on the MVCT for that day in the X, Y and Z directions was found to be 1.93 cm (+/-1.5), 4.6 cm (+/-1.03) and 0.654 cm (+/-0.35), respectively. CONCLUSIONS: Endobiliary stents are stable tumour localisation surrogates and can be used to correct for interfraction target motion.

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[281]

TÍTULO / TITLE: - Management of a patient diagnosed with pancreatic cancer and myelodysplastic syndrome.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Gastrointest Cancer Res. 2013 Mar;6(2):56-60.
AUTORES / AUTHORS: - Won E; Yu KH; Shamseddine A; Saltz L; Mukherjee D; Haydar A; El-Olayan A; Temraz S; Naghy M; Makanjoula D; O'Reilly EM; Abou-Alfa GK
INSTITUCIÓN / INSTITUTION: - Memorial Sloan-Kettering Cancer Center New York, NY.

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[282]
TÍTULO / TITLE: - Role of Peroxisome Proliferator-Activated Receptor beta/delta and B-Cell Lymphoma-6 in Regulation of Genes Involved in Metastasis and Migration in Pancreatic Cancer Cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PPAR Res. 2013;2013:121956. doi: 10.1155/2013/121956. Epub 2013 May 2.
●● Enlace al texto completo (gratuito o de pago) 1155/2013/121956
AUTORES / AUTHORS: - Coleman JD; Thompson JT; Smith RW 3rd; Prokopczyk B; Vanden Heuvel JP
INSTITUCIÓN / INSTITUTION: - Department of Veterinary and Biomedical Sciences and Center for Molecular Toxicology and Carcinogenesis, Penn State University, 325 Life Sciences Building, University Park, PA 16802, USA.
RESUMEN / SUMMARY: - PPARbeta/delta is a ligand-activated transcription factor that regulates various cellular functions via induction of target genes directly or in concert with its associated transcriptional repressor, BCL-6. Matrix remodeling proteinases are frequently over-expressed in pancreatic cancer and are involved with metastasis. The present study tested the hypothesis that PPARbeta/delta is expressed in human pancreatic cancer cells and that its activation could regulate MMP-9, decreasing cancer cells ability to transverse the basement membrane. In human pancreatic cancer tissue there was significantly higher expression of MMP-9 and PPARbeta/delta, and lower levels of BCL-6 mRNA. PPARbeta/delta activation reduced the TNF alpha -induced expression of various genes implicated in metastasis and reduced the invasion through a basement membrane in cell culture models. Through the use of short hairpin RNA inhibitors of PPARbeta/delta, BCL-6, and MMP-9, it was evident that PPARbeta/delta was responsible for the ligand-dependent effects whereas BCL-6 dissociation upon GW501516 treatment was ultimately responsible for decreasing MMP-9 expression and hence invasion activity. These results suggest that PPARbeta/delta plays a role in regulating pancreatic cancer cell invasion through regulation of genes via ligand-dependent release of BCL-6 and that activation of the receptor may provide an alternative therapeutic method for controlling migration and metastasis.

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[283]
TÍTULO / TITLE: - Caudal pancreatic tumour in a young patient.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Diagn Interv Imaging. 2013 May 28. pii: S2211-5684(13)00137-X. doi: 10.1016/j.diii.2013.04.004.
●● Enlace al texto completo (gratuito o de pago) 1016/j.diii.2013.04.004
AUTORES / AUTHORS: - Klotz T; Da Ines D; Petitcolin V; Lannareix V; Essamet W; Garcier JM
INSTITUCIÓN / INSTITUTION: - Department of Radiology and Medical Imaging, CHU Clermont-Ferrand, CHU Estaing, 1, place Lucie-Aubrac, 63003 Clermont-Ferrand cedex 1, France.

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[284]
TÍTULO / TITLE: - The role of Endoscopic Ultrasound (EUS) in the management of patients with pancreatic cancer: now bigger than ever.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Gastrointest Oncol. 2013 Jun;4(2):121-2. doi: 10.3978/j.issn.2078-6891.2013.009.
●● Enlace al texto completo (gratuito o de pago) 3978/j.issn.2078-6891.2013.009
AUTORES / AUTHORS: - Isayama H; Nakai Y; Draganov PV
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan;

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[285]
TÍTULO / TITLE: - Risk factors for the occurrence of insulinoma: a case-control study.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Hepatobiliary Pancreat Dis Int. 2013 Jun;12(3):324-8.
AUTORES / AUTHORS: - Zhan HX; Cong L; Zhao YP; Zhang TP; Chen G
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing 100730, China. zhao8028@263.net
RESUMEN / SUMMARY: - BACKGROUND: The etiology of insulinoma is poorly understood. Few studies investigated the possible roles of environmental factors and lifestyle in the pathogenesis of insulinoma. The aim of this study is to identify risk factors associated with occurrence of insulinoma in the Chinese population. METHODS: This study consisted of 196 patients with insulinoma and 233 controls. Demographic information of the patients and controls and risk factors of the disease were analyzed. Univariate and unconditional multivariable logistic regression analyses were made to estimate odds ratios (ORs) and possible risk factors. RESULTS: Approximately 68.88% (135/196) of the patients were from rural areas in contrast to 10.30% (24/233) of the controls (P<0.0001). This difference was confirmed by the multivariate analysis

(OR=4.950; 95% CI: 2.928-8.370). Family history of pancreatic endocrine tumor (OR=16.754; 95% CI: 2.125-132.057) and other cancers (OR=2.360; 95% CI: 1.052-5.291) was also related to a high-risk population of insulinoma. CONCLUSION: Rural residents or people who have a family history of pancreatic endocrine tumor and other cancers are a high-risk population of insulinoma.

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[286]

TÍTULO / TITLE: - The estimation of metaloproteinases and their inhibitors blood levels in patients with pancreatic tumors.

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

REVISTA / JOURNAL: - World J Surg Oncol. 2013 Jun 14;11:137. doi: 10.1186/1477-7819-11-137.

●● Enlace al texto completo (gratuito o de pago) 1186/1477-7819-11-137

AUTORES / AUTHORS: - Smigielski J; Piskorz L; -Wojnarowska RT; Malecka-Panas E; Jablonski S; Brocki M

INSTITUCIÓN / INSTITUTION: - Department of Thoracic, General and Oncological Surgery, Medical University, 113 Zeromskiego Street, 90-549 Lodz, Poland. jacek.smigielski@umed.lodz.pl

RESUMEN / SUMMARY: - BACKGROUND: The aim of the study was to evaluate the concentration of proteolytic enzymes, MMP-2 and MMP-9, and their tissue inhibitors, TIMP-1 and TIMP-2, in the blood of patients with benign and malignant pancreatic tumors. METHODS: MMP-2, MMP-9, TIMP-1, and TIMP-2 were evaluated in the patients with benign and malignant pancreatic tumors before surgery and in the 30-day follow-up. The study covered 134 patients aged 54 to 76 years, who were divided into groups by TNM staging. RESULTS: Before the operation, the highest mean concentration of MMP-2 was found in patients with unresectable cancer, whereas the highest level of MMP-9 was in patients with resectable cancer. The highest level of TIMP-1 was noted in patients with inflammatory tumors. In 1 month following the operation, the highest level of MMP-2 was also in patients with unresectable cancer and the highest level of TIMP-2 in patients with inflammatory tumors. CONCLUSIONS: The evaluation of the level of the studied cytokines in the pancreatic tumor patients can be diagnostically significant in the differentiation of benign and malignant changes. The changes in the levels of the studied enzymes and their inhibitors can have a prognostic value in the clinical severity of pancreatic cancer.

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[287]

TÍTULO / TITLE: - Impact of body mass index for patients undergoing pancreaticoduodenectomy.

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

REVISTA / JOURNAL: - World J Gastrointest Pathophysiol. 2013 May 15;4(2):37-42. doi: 10.4291/wjgp.v4.i2.37.

●● Enlace al texto completo (gratuito o de pago) 4291/wjgp.v4.i2.37

AUTORES / AUTHORS: - Del Chiaro M; Rangelova E; Ansorge C; Blomberg J; Segersvard R

INSTITUCIÓN / INSTITUTION: - Marco Del Chiaro, Elena Rangelova, Christoph Ansorge, John Blomberg, Ralf Segersvard, Division of Surgery, Department of Clinical Science, Intervention and Technology, Karolinska Institute at Karolinska University Hospital, 14186 Stockholm, Sweden.

RESUMEN / SUMMARY: - AIM: To evaluate the impact of body mass index (BMI) on short and long term results after pancreaticoduodenectomies (PD). METHODS: A consecutive series of PDs performed at the Karolinska University Hospital from 2004 till 2010 were retrieved from our prospective database. The patients were divided by BMI into overweight/obese (O; BMI >/= 25 kg/m(2)) and controls (C; BMI < 25 kg/m(2)). Demographics, peri-operative data, morbidity, mortality, pancreatic fistula (PF) rate, length of stay (LOS), hospital costs, histology, and survival were analyzed. An additional sub analysis of survival was performed in patients with a diagnosis of pancreatic ductal adenocarcinoma (PDAC) and divided in underweight, normal-weight, overweight and obese. RESULTS: A total of 367 PDs were included (O = 141/C = 226). No differences were found between O and C regarding demographics, peri-operative data, costs, morbidity or mortality. O was associated with higher intra-operative blood loss (1392 +/- 115 mL vs 1121 +/- 83 mL; P = 0.01), rate of PF (20% vs 9.5%; P = 0.006) and marginally longer LOS (18 +/- 0.9 d vs 15 +/- 1.1 d; P = 0.05). An increasing risk for PF was observed with increasing BMI. The 1, 3 and 5 years survival rate was similar in O and C in PDAC (68.7%, 26.4% and 8.8% vs 66.1%, 30.9% and 17.9% respectively; P = 0.9). When the survival was analyzed using 4 different categories of BMI (underweight, normal, overweight and obese), a trend was seen toward a difference in survival, with a worse prognosis for the underweight and obese patients compared to normal weight and overweight patients. CONCLUSION: Overweight increases the risk for intra-operative bleeding and PF, but do not otherwise alter short or long term outcome after PD for pancreatic cancer.

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[288]

TÍTULO / TITLE: - Re-evaluation of ABO gene polymorphisms detected in a genome-wide association study and risk of pancreatic ductal adenocarcinoma in a Chinese population.

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

REVISTA / JOURNAL: - Chin J Cancer. 2013 Jul 2. doi: 10.5732/cjc.013.10060.

●● Enlace al texto completo (gratuito o de pago) 5732/cjc.013.10060

AUTORES / AUTHORS: - Xu HL; Cheng JR; Zhang W; Wang J; 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 200032, P.R. China. ytgao@vip.sina.com.

RESUMEN / SUMMARY: - Pancreatic cancer is a fatal malignancy with an increasing incidence in Shanghai, China. A genome-wide association study (GWAS) and other work have shown that ABO alleles are associated with pancreatic cancer risk. We conducted a population-based case-control study involving 256 patients with pathologically confirmed pancreatic ductal adenocarcinoma (PDAC) and 548 healthy controls in Shanghai, China, to assess the relationships between GWAS-identified ABO alleles and risk of PDAC. Carriers of the C allele of rs505922 had an increased cancer risk [adjusted odds ratio (OR) = 1.42, 95% confidence interval (CI): 1.02-1.98] compared to TT carriers. The T alleles of rs495828 and rs657152 were also significantly associated with an elevated cancer risk (adjusted OR = 1.58, 95% CI: 1.17-2.14; OR = 1.51, 95% CI: 1.09-2.10). The rs630014 variant was not associated with risk. We did not find any significant gene-environment interactions with cancer risk using a multifactor dimensionality reduction (MDR) method. Haplotype analysis also showed that the haplotype CTTC was associated with an increased risk of PDAC (adjusted OR = 1.46, 95% CI: 1.12-1.91) compared with haplotype TGGT. GWAS-identified ABO variants are thus also associated with risk of PDAC in the Chinese population.

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[289]

TÍTULO / TITLE: - Prognostic value of somatostatin receptor-2 positivitiy in gastroenteropancreatic neuroendocrine tumors in reference to known prognostic factors.

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

REVISTA / JOURNAL: - Turk J Gastroenterol. 2012 Dec;23(6):736-40.

AUTORES / AUTHORS: - Yeniay L; Gurcu BI; Unalp O; Yilmaz F; Nart D; Sozbilen M; Coker A

INSTITUCIÓN / INSTITUTION: - Ege University School of Medicine, Department of General Surgery, Izmir, Turkey E-Mail: lyeniay@yahoo.com.

RESUMEN / SUMMARY: - Background/aims:Identification of the predictive factors for the prognosis of gastroenteropancreatic neuroendocrine tumors is important but rather challenging due to the rarity of the condition. This study aimed to examine the association between somatostatin receptor-2 positivity and known prognostic factors for gastroenteropancreatic neuroendocrine tumor to identify the value ofsomatostatin receptor-2 positivity itself as a predictive factor for prognosis. Materials and Methods: Records of 41 gastroenteropancreatic neuroendocrine tumor patients (24 females, 17 males) were retrospectively reviewed. The relations between somatostatin eceptor-2 positivity and known prognostic factors including tumor stage, Ki-67 positivity, vascular or perineural invasion, lymph node metastasis, presence of necrosis, and soft tissue extension were analyzed. Results:Sixty percent of the patients had histologically

confirmed somatostatin receptor-2 positivity with 45% exhibiting focal and 15% showing diffuse staining characteristic. No significant relation was found between somatostatin receptor-2 positivity and any of the known prognostic factors for gastroenteropancreatic neuroendocrine tumor: versus stage, p=0.67; vs. lymph node metastasis, p=0.51; vs. vascular invasion, p=0.11; vs. extension to surrounding soft tissue, p=0.54; vs. necrosis, p=0.23; vs. lymphatic invasion, p=0.25; and vs. perineural invasion, p=0.42. Conclusions:Somatostatin receptor-2 positivity, either focal or diffuse, does not seem to predict prognosis in gastroenteropancreatic neuroendocrine tumors. However, growing evidence supports the benefits of somatostatin analogues as adjunctive treatment in this group of patients.

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[290]

TÍTULO / TITLE: - Standard versus extended pancreaticoduodenectomy in treating adenocarcinoma of the head of the pancreas.

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

REVISTA / JOURNAL: - Chin Med Sci J. 2013 Jun;28(2):107-12.

AUTORES / AUTHORS: - Gong J; Mai G; Zheng ZJ; Xiang GM; Hu WM; Tian BL; Zhang ZD; Liu XB

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary and Pancreatic Surgery, Sichuan Academy of Medical Science and Sichuan Provincial People's Hospital, Chengdu 610072, China.

RESUMEN / SUMMARY: - OBJECTIVES: To compare the postoperative complications and survival of standard pancreatoduodenectomy (SPD) and extended pancreatoduodenectomy (EPD) in patients with resectable adenocarcinoma of the head of the pancreas. METHODS: Between January 1994 and December 2011, 165 patients with biopsy-proven adenocarcinoma of the pancreatic head were treated in West China Hospital, among whom 93 underwent SPD and 72 had EPD. Complications and survival after the surgery were analyzed retrospectively. RESULTS: The median operation time of the EPD group was longer compared with the SPD group (375 minutes vs.310 minutes, P<0.01), the volume of blood transfusion was larger (700 mL vs.400 mL, P<0.05), while the median hospital stay (13.5 days vs.12 days, P=0.79) and the total complication rates were comparable (34.7% vs.32.4%, P=0.93). The total recurrence rates of the SPD and EPD groups were not significantly different (52.7% vs. 43.1%, P=0.83). No significant differences were found between the SPD and EPD groups in 1-year (81.7% vs. 86.1%), 3-year (38.7% vs. 43.1%), 5-year (16.7% vs. 19.4%), and median survivals (19.8 months vs. 23.2 months, P= 0.52). CONCLUSION: The postoperative complications and survival donot differ significantly between SPD and EPD.

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[291]

TÍTULO / TITLE: - Non-pancreatic retroperitoneal pseudocyst: a benign disease with non-specific symptoms.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - British Medical J (BMJ). %8?(3k+]3s http://bmj.com/search.dtl ●● British Medical J. (BMJ): <> Case Rep. 2013 Jul 2;2013. pii: bcr2013200184. doi: 10.1136/bcr-2013-200184.
●● Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-200184
AUTORES / AUTHORS: - Prabhu R; Rodrigues G; Sarma YS; Benakatti R
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Kasturba Medical College, Manipal, Karnataka, India. drraghu81@yahoo.co.in
RESUMEN / SUMMARY: - A 76-year-old man presented with abdominal pain and constipation for 1 month. The pain was dull aching in nature and over the right upper abdomen. He also reported decreased appetite. The patient had no previous attacks of acute pancreatitis or history of trauma. There was no history of fever or melena. On visual inspection of the abdomen, there was a mass effect protruding out of the right mid-abdomen. The mass was approximately measuring 15x15 cm, firm in consistency, non-tender, non-mobile and not moving with respiration. Haematological investigations were normal. Both amylase and lipase were within normal limits. A CT of the abdomen revealed a large well-defined thin-walled cystic lesion measuring 10.3x13.9x14.3 cm in the right lumbar and iliac region without calcification or haemorrhage. A diagnosis of retroperitoneal cyst was made and the patient was taken up for surgery. Histology of the cyst showed the absence of epithelia and was reported as pseudocyst.

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[292]
TÍTULO / TITLE: - A late recurrence of renal cell carcinoma as pancreatic metastases: a rare disease.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - British Medical J (BMJ). %8?(3k+]3s http://bmj.com/search.dtl ●● British Medical J. (BMJ): <> Case Rep. 2013 May 31;2013. pii: bcr2013009314. doi: 10.1136/bcr-2013-009314.
●● Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-009314
AUTORES / AUTHORS: - Kapoor R; Kumar R; Dey P; Mittal BR
INSTITUCIÓN / INSTITUTION: - Department of Radiotherapy and Oncology, Post Graduate Institute of Medical Education and Research, Chandigarh, Chandigarh, India. drkapoor.r@gmail.com
RESUMEN / SUMMARY: - A man presented with multifocal pancreatic metastases 9 years after nephrectomy for renal cell carcinoma. He was managed with oral sunitinib. He had favourable response to treatment with excellent compliance.

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[293]
TÍTULO / TITLE: - Oncogenesis and the Clinical Significance of K-ras in Pancreatic Adenocarcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(5):2699-701.
AUTORES / AUTHORS: - Huang C; Wang WM; Gong JP; Yang K
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Three Gorges Medical College, Chongqing, China E-mail : Johnniu00@163.com.
RESUMEN / SUMMARY: - The RAS family genes encode small GTP-binding cytoplasmic proteins. Activated KRAS engages multiple effector pathways, notably the RAF-mitogen-activated protein kinase, phosphoinositide-3-kinase (PI3K) and RalGDS pathways. In the clinical field, K-ras oncogene activation is frequently found in human cancers and thus may serve as a potential diagnostic marker for cancer cells in circulation. This mini-review aims to summarise information on Ras-induced oncogenesis and the clinical significance of K-ras.

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[294]
TÍTULO / TITLE: - miR203 regulates the proliferation, apoptosis and cell cycle progression of pancreatic cancer cells by targeting Survivin.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Mol Med Rep. 2013 Aug;8(2):379-84. doi: 10.3892/mmr.2013.1504. Epub 2013 May 31.
●● Enlace al texto completo (gratuito o de pago) 3892/mmr.2013.1504
AUTORES / AUTHORS: - Xu D; Wang Q; An Y; Xu L
INSTITUCIÓN / INSTITUTION: - Department of General Surgery, The Second Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu 210018, P.R. China.
RESUMEN / SUMMARY: - MicroRNAs have emerged as crucial regulators of tumorigenesis. However, the mechanism by which miR203 is involved in the pathogenesis of pancreatic cancer (PC) remains elusive. In the present study, PC cell lines were used as an experimental model to investigate the expression and functional role of miR203 in PC. miR203 mimic virus, miRNA negative control virus and Survivin shRNA virus were transfected into the PC cell line, CFPAC1. mRNA and protein levels of Survivin were detected using qPCR and western blot analysis. Proliferation, apoptosis and cell cycle profiles were detected by an MTT assay and flow cytometry. Female BALB/cAnu nude mice were used to validate the role of miR203 in vivo. The protein levels of Survivin were found to negatively correlate with miR203 levels in four PC cell lines. A luciferase assay revealed that Survivin was a direct target of miR203. Transfection with miR203 mimic inhibited CFPAC1 cell proliferation and induced apoptosis and G1 phase cell cycle arrest, similar to knockdown of Survivin. In the in vivo nude mouse model, the downregulation of Survivin by knockdown of Survivin or transfection with miR203 mimic inhibited tumor growth. Results of the current study indicate that miR203 regulates the proliferation, apoptosis and cell cycle progression of PC cells by targeting Survivin.

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[295]
TÍTULO / TITLE: - Association of vitamin D receptor gene polymorphisms with pancreatic cancer: A pilot study in a North China Population.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Oncol Lett. 2013 May;5(5):1731-1735. Epub 2013 Feb 28.
●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1215
AUTORES / AUTHORS: - Li L; Wu B; Yang L; Yin G; Wei W; Sui S; Liu J
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Shandong Provincial Hospital, Shandong University, Jinan 250021; ; Department of Internal Medicine, Taian City Central Hospital, Taian 271000, P.R. China.
RESUMEN / SUMMARY: - Polymorphisms of the vitamin D receptor (VDR) gene may be a risk factor for pancreatic cancer (PC). We investigated the association of two single-nucleotide polymorphisms (SNPs) of the VDR gene with PC in age- and gender-matched patients and controls. PC (n=91) and healthy control (n=80) samples were genotyped for the FokI (rs2228570) and BsmI (rs1544410) polymorphisms using the PCR and restriction fragment length polymorphism (PCR-RFLP) method. Chi-square analysis was used to test for the overall association of VDR genotype with disease. There was a significant difference in the frequency of genotype FF between the PC patients and controls (Ptrend=0.009); however, the difference in frequency of genotype BB between the two groups was not significant (Ptrend=0.082). The difference between FF and Ff/ff frequency was significant (P=0.002). The two high-risk genotypes were ffbb and Ffbb, with an 11.66- and 6.42-fold increased risk of PC, respectively. VDR gene polymorphisms were important for the development of PC in this study population; however, further exploration of these findings and their implications are required.

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[296]
TÍTULO / TITLE: - Association between variations in the fat mass and obesity-associated gene and pancreatic cancer risk: a case-control study in Japan.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - BMC Cancer. 2013 Jul 8;13:337. doi: 10.1186/1471-2407-13-337.
●● Enlace al texto completo (gratuito o de pago) 1186/1471-2407-13-337
AUTORES / AUTHORS: - Lin Y; Ueda J; Yagyu K; Ishii H; Ueno M; Egawa N; Nakao H; Mori M; Matsuo K; Kikuchi S
INSTITUCIÓN / INSTITUTION: - Department of Public Health, Aichi Medical University School of Medicine, Nagakute, Aichi, Japan.
RESUMEN / SUMMARY: - BACKGROUND: It is clear that genetic variations in the fat mass and obesity-associated (FTO) gene affect body mass index and the risk of obesity. Given the mounting evidence showing a positive association between obesity and pancreatic cancer, this study aimed to investigate the relation between variants in the FTO gene, obesity and pancreatic cancer risk.

METHODS: We conducted a hospital-based case-control study in Japan to investigate whether genetic variations in the FTO gene were associated with pancreatic cancer risk. We genotyped rs9939609 in the FTO gene of 360 cases and 400 control subjects. An unconditional logistic model was used to estimate the odds ratio (OR) and 95% confidence interval (CI) for the association between rs9939609 and pancreatic cancer risk. RESULTS: The minor allele frequency of rs9939609 was 0.18 among control subjects. BMI was not associated with pancreatic cancer risk. Compared with individuals with the common homozygous TT genotype, those with the heterozygous TA genotype and the minor homozygous AA genotype had a 48% (OR=1.48; 95%CI: 1.07-2.04), and 66% increased risk (OR=1.66; 95%CI: 0.70-3.90), respectively, of pancreatic cancer after adjustment for sex, age, body mass index, cigarette smoking and history of diabetes. The per-allele OR was 1.41 (95%CI: 1.07-1.85). There were no significant interactions between TA/AA genotypes and body mass index. CONCLUSIONS: Our findings indicate that rs9939609 in the FTO gene is associated with pancreatic cancer risk in Japanese subjects, possibly through a mechanism that is independent of obesity. Further investigation and replication of our results is required in other independent samples.

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[297]

TÍTULO / TITLE: - Inhibition of transketolase by oxythiamine altered dynamics of protein signals in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Exp Hematol. %8?(3k+]3s http://www.medicinedirect.com/journal ●● Experimental Hematology: <> Oncol. 2013 Jul 27;2(1):18.

●● Enlace al texto completo (gratuito o de pago) 1186/2162-3619-2-18

AUTORES / AUTHORS: - Wang J; Zhang X; Ma D; Lee WN; Xiao J; Zhao Y; Go VL; Wang Q; Yen Y; Recker R; Xiao GG

RESUMEN / SUMMARY: - Oxythiamine (OT), an analogue of anti-metabolite, can suppress the nonoxidative synthesis of ribose and induce cell apoptosis by causing a G1 phase arrest in vitro and in vivo. However, the molecular mechanism remains unclear yet. In the present study, a quantitative proteomic analysis using the modified SILAC method (mSILAC) was performed to determine the effect of metabolic inhibition on dynamic changes of protein expression in MIA PaCa-2 cancer cells treated with OT at various doses (0 muM, 5 muM, 50 muM and 500 muM) and time points (0 h, 12 h and 48 h). A total of 52 differential proteins in MIA PaCa-2 cells treated with OT were identified, including 14 phosphorylated proteins. Based on the dynamic expression pattern, these proteins were categorized in three clusters, straight down-regulation (cluster 1, 37% of total proteins), upright “V” shape expression pattern (cluster 2, 47.8% total), and downright “V” shape pattern (cluster 3, 15.2% total). Among them, Annexin A1 expression was significantly down-

regulated by OT treatment in time-dependent manner, while no change of this protein was observed in OT dose-dependent fashion. Pathway analysis suggested that inhibition of transketolase resulted in changes of multiple cellular signaling pathways associated with cell apoptosis. The temporal expression patterns of proteins revealed that OT altered dynamics of protein expression in time-dependent fashion by suppressing phosphor kinase expression, resulting in cancer cell apoptosis. Results from this study suggest that interference of single metabolic enzyme activity altered multiple cellular signaling pathways.

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[298]

TÍTULO / TITLE: - MUC1 induces drug resistance in pancreatic cancer cells via upregulation of multidrug resistance genes.

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

REVISTA / JOURNAL: - Oncogenesis. 2013 Jun 17;2:e51. doi: 10.1038/oncsis.2013.16.

●● Enlace al texto completo (gratuito o de pago) 1038/oncsis.2013.16

AUTORES / AUTHORS: - Nath S; Daneshvar K; Roy LD; Grover P; Kidiyoor A; Mosley L; Sahraei M; Mukherjee P

INSTITUCIÓN / INSTITUTION: - Department of Biology, University of North Carolina at Charlotte, Charlotte, NC, USA.

RESUMEN / SUMMARY: - MUC1 (CD227), a membrane tethered mucin glycoprotein, is overexpressed in >60% of human pancreatic cancers (PCs), and is associated with poor prognosis, enhanced metastasis and chemoresistance. The objective of this study was to delineate the mechanism by which MUC1 induces drug resistance in human (BxPC3 and Capan-1) and mouse (KCKO, KCM) PC cells. We report that PC cells that express high levels of MUC1 exhibit increased resistance to chemotherapeutic drugs (gemcitabine and etoposide) in comparison with cells that express low levels of MUC1. This chemo resistance was attributed to the enhanced expression of multidrug resistance (MDR) genes including ABCC1, ABCC3, ABCC5 and ABCB1. In particular, levels of MRP1 protein encoded by the ABCC1 gene were significantly higher in the MUC1-high PC cells. In BxPC3 and Capan-1 cells MUC1 upregulates MRP1 via an Akt-dependent pathway, whereas in KCM cells MUC1-mediated MRP1 upregulation is via an Akt-independent mechanism. In KCM, BxPC3 and Capan-1 cells, the cytoplasmic tail motif of MUC1 associates directly with the promoter region of the Abcc1/ABCC1 gene, indicating a possible role of MUC1 acting as a transcriptional regulator of this gene. This is the first report to show that MUC1 can directly regulate the expression of MDR genes in PC cells, and thus confer drug resistance.

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[299]

TÍTULO / TITLE: - A case of anaplastic carcinoma of pancreas diagnosed with endoscopic ultrasound-guided fine needle aspiration cytology.

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

REVISTA / JOURNAL: - Turk J Gastroenterol. 2012 Dec;23(6):828-9.
AUTORES / AUTHORS: - Ergun M; Aydog G; Kayacetin E; Sasmaz N
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Turkiye Yuksek Ihtisas Hospital, Ankara, Turkey.
RESUMEN / SUMMARY: - Anaplastic carcinoma of the pancreas is a rare and very aggressive tumor. It accounts for 2-7% of all pancreatic malignancies and occurs usually in older male patients (1,2). Three major histologic types have been described: spindle cell, sarcomatoid and pleomorphic carcinoma (3). While diagnosis can be made with surgical excision or surgical biopsy, diagnosis with endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) biopsy has become useful to obtain tissue samples in order to recognize this distinct entity. There have been only a few reports describing diagnosis of anaplastic carcinoma with EUS-FNA (4-6). A 60-year-old male was admitted complaining of abdominal pain, nausea, vomiting, and weight loss (8 kg/3 months). The patient had jaundice and had been examined in another center two weeks before, and was referred to us after placement of a plastic stent in the common bile duct. Laboratory investigations revealed hemoglobin (Hb): 12 g/L, total/direct bilirubin: 2.5/1.9 mg/dl, CEA: 8.5 (0-3.4) ng/ml, and CA19-9: 218.7 (<39) U/ml. Transabdominal US showed suspected pancreatic mass lesion, and abdominal computed tomography (CT) revealed a hypoechoic mass lesion in the head of the pancreas. Thin-section pancreatic-phase sequence showed circumferential encasement of the celiac axis as well as hepatic artery and peripancreatic lymphadenopathies. Tumor stage was determined as T4N1M0 and classified as unresectable. The pancreatic duct measured 5 mm at the body of the pancreas. EUS showed a hypoechoic, heterogeneous mass lesion (26x32 mm) in the pancreatic head and peripancreatic lymphadenopathies (Figure 1). EUS-FNA was performed to obtain histological confirmation of the lesion. Cytologically, the tumor, which consisted of distinctive pleomorphic cells, was diagnosed as an anaplastic carcinoma (Figure 2). The patient received two cycles of chemotherapy (gemcitabine). He had stent exchange due to occlusion of the stent at the common bile duct. He is still alive four months after the diagnosis. Anaplastic carcinoma of the pancreas is a rare and very aggressive tumor with survival prognosis oF several months. A variety of terms have been used to describe these tumors, including undifferentiated or pleomorphic carcinoma, pleomorphic giant cell carcinoma, small cell carcinoma, and sarcomatoid carcinoma (2,3). Weight loss, fatigue, loss of appetite, abdominal pain, nausea, and vomiting are the usual clinical presenting symptoms. There are two large series of anaplastic pancreatic carcinoma in the literature. Paal et al. (2) and Khashab et al. (4) described 35 and 13 anaplastic carcinomas of the pancreas, respectively. Paal's study was based on pathologic specimens of surgical materials, whereas in Khashab's study, the diagnosis was performed with cytologic samples of EUS-FNA biopsies (n=5) and surgical pathologies. There are also a limited number of case reports of anaplastic carcinoma diagnosed with EUS-FNA biopsy (5,6).

Our case could be diagnosed based on cytologic examination obtained from the FNA biopsy. Cytopathologic examination revealed undifferentiated carcinoma with bizarre, pleomorphic cells in addition to spindle-shaped sarcomatous cells. EUS-FNA has become a widely accepted modality for the tissue diagnosis of pancreatic lesions. Moreover, EUS-FNA of pancreatic masses is safe and has an overall accuracy of 90% (7). EUS-FNA plays an important role in differentiating ductal carcinoma from other rare pancreatic mass lesions such as small cell carcinoma and pancreatic lymphoma, and from benign conditions like autoimmune pancreatitis, although the necessity of obtaining a cytologic or tissue diagnosis in pancreatic cancer prior to surgery remains controversial and is highly dependent on the institution (8). Arguments in favor of preoperative biopsy include its ability to provide proof of pathology prior to surgery, to exclude unusual pathologies, and to provide evidence of disease before the initiation of a multidisciplinary treatment, such as neoadjuvant chemotherapy. There can be only one potential problem for EUS-FNA, i.e. tumor seeding, but it is a very rare entity, with only two case reports at present (9,10). For unresectable cases, histologic confirmation and typing are absolutely necessary for chemotherapy. Although there are some CT and EUS features for discriminating between malignant and benign processes, their ability is limited, and EUS-FNA is one of the best procedures for obtaining a tissue diagnosis. Anaplastic carcinoma usually presents with giant mass lesion, and diagnosis is based on histology. In our case, the patient presented with jaundice, which enabled the definition of early diagnosis and better survival. Definitive diagnosis was made by EUS-FNA. Anaplastic pancreas carcinomas are associated with poorer survival when compared to invasive ductal adenocarcinomas. Neither curative resection nor chemotherapy or radiotherapy has been shown to have any benefit due to the aggressive nature and rapid recurrence rates of the disease (11). Palliative care and close monitoring are the only therapeutic options in most of the cases. Treatment alternatives for this dismal disease remain to be defined.

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[300]

TÍTULO / TITLE: - The S100A8/A9 complex reduces CTLA4 expression by immature myeloid cells: Implications for pancreatic cancer-driven immunosuppression.

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

REVISTA / JOURNAL: - Oncoimmunology. 2013 Jun 1;2(6):e24441. Epub 2013 May 9.

●● Enlace al texto completo (gratuito o de pago) 4161/onci.24441

AUTORES / AUTHORS: - Basso D; Fogar P; Plebani M

INSTITUCIÓN / INSTITUTION: - Department of Laboratory Medicine; University-Hospital of Padova; Padova, Italy.

RESUMEN / SUMMARY: - An expansion of different myeloid derived suppressive cell (MDSC) subsets can be detected in the blood and secondary lymphoid organs of early and advanced pancreatic ductal adenocarcinoma (PDAC) patients. Double negative (CD14-HLA-DR-) MDSCs are frequently induced by PDACs. In addition, by releasing S100A8 and S100A9, advanced PDAC lesions cause an expansion of highly immunosuppressive CD33+CD14+HLA-DR- monocytic MDSCs expressing low levels of cytotoxic T lymphocyte antigen 4 (CTLA4) on the cell surface.

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[301]

TÍTULO / TITLE: - Chronic intermittent hypoxia increases beta cell mass and activates the mammalian target of rapamycin/hypoxia inducible factor 1/vascular endothelial growth factor A pathway in mice pancreatic islet.

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

REVISTA / JOURNAL: - Chin Med J (Engl). 2013 Jun;126(12):2368-73.

AUTORES / AUTHORS: - Gu CJ; Li M; Li QY; Li N

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Shanghai Ruijin Hospital, Medical School of Shanghai Jiao Tong University, Shanghai 200025, China.

RESUMEN / SUMMARY: - BACKGROUND: Growing evidence from population and clinic based studies showed that obstructive sleep apnea (OSA) and its characterizing chronic intermittent hypoxia (IH) were independently associated with the development of type 2 diabetes mellitus. However, the pathogenesis by which OSA induces glucose metabolic disorders is not clear. We determined changes in pancreatic beta cell mass and the mammalian target of rapamycin (mTOR)/hypoxia inducible factor 1 (HIF-1)/vascular endothelial growth factor A (VEGF-A) pathway following IH exposure. METHODS: A controlled gas delivery system regulated the flow of nitrogen and oxygen into a customized cage housing mice during the experiment. Twenty-four male wild C57BL/6J mice were either exposed to IH (n = 12) or intermittent air as a control (n = 12) for 56 days. Mice were anaesthetized and sacrificed after exposure, pancreas samples were dissected for immunofluorescent staining. Insulin and DAPI staining labelled islet beta cells. Insulin positive area and beta cell number per islet were measured. P-S6, HIF-1alpha and VEGF-A staining were performed to detect the activation of mTOR/HIF-1/VEGF-A pathway. RESULTS: After eight weeks of IH exposure, insulin positive area increased by an average of 18.5% ($P < 0.05$). The beta cell number per islet increased (92 vs. 55, respectively for IH and the control groups, $P < 0.05$) with no change in the size of individual beta cells. Islet expression of HIF-1alpha and VEGF-A were higher in IH group than control group, and percentage of p-S6 positive beta cell also increased after IH exposure (16.8% vs. 4.6% respectively for IH and the control groups, $P < 0.05$). CONCLUSION: The number of pancreatic beta cells increased as did the activity of the mTOR/HIF-1/VEGF-A pathway after exposure to IH.

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[302]

TÍTULO / TITLE: - Novel agents and future prospects in the treatment of pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):395-400. doi: 10.6092/1590-8577/1654.

AUTORES / AUTHORS: - Sarris EG; Syrigos KN; Saif MW

INSTITUCIÓN / INSTITUTION: - Oncology Unit, Third Department of Medicine, University of Athens, Sotiria General Hospital. Athens, Greece. sarris_v@yahoo.gr.

RESUMEN / SUMMARY: - Pancreatic adenocarcinoma is one of the most aggressive malignancies and the fourth leading cause of cancer-related mortality in the United States. The majority of patients are diagnosed at advanced stage with inoperable locally advanced tumors or metastatic disease, and palliative chemotherapy remains the best therapeutic option for these patients. Despite intensive clinical and pre-clinical research over the last few years, the combination of the anti-metabolite drug gemcitabine with the targeted agent erlotinib, is considered standard of care in the treatment of these patients, with only minimal or modest efficacy. Therefore, novel therapeutic approaches are currently under clinical investigation in an attempt to produce more definite results for this fatal disease. In this paper we summarize five most interesting research abstracts as presented at the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting. In two studies, nimotuzumab, a monoclonal antibody against epidermal growth factor receptor (EGFR) (Abstract #4009) and bavituximab, a monoclonal antibody against phosphatidylserine (Abstract #4054) are tested in combination with gemcitabine in patients with advanced pancreatic cancer. Abstract #4012 is a study of gemcitabine with vismodegib, a novel hedgehog pathway inhibitor, whereas in Abstract #4035, toxicity and efficacy results of sunitinib in combination with gemcitabine in patients with pancreatic adenocarcinoma are presented. Lastly, safety results of pimasertib, a novel mitogen-activated protein kinase kinase (MEK) inhibitor, combined with the standard gemcitabine are presented in Abstract #4041.

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[303]

TÍTULO / TITLE: - Splenomegaly as the first manifestation of pancreatic adenosquamous carcinoma: A case report.

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

REVISTA / JOURNAL: - Turk J Gastroenterol. 2012 Dec;23(6):799-803.

AUTORES / AUTHORS: - Mou YP; Chen K; Xu XW; Xie K; Zhou YC

INSTITUCIÓN / INSTITUTION: - Sie Run Run Shaw Hospital, Department of General Surgery, Hangzhou Zhejiang Province, China.

RESUMEN / SUMMARY: - Adenosquamous carcinoma of the pancreas directly invading surrounding organs is rare. Here, we describe a case of pancreatic

adenosquamous carcinoma directly invading the spleen and colon in a 44-year-old man. Imaging examinations revealed a huge heterogeneous mass in the enlarged spleen and a colonic lump, but showed no obvious space-occupying lesion in the pancreas. An exploratory laparotomy revealed that the enlarged spleen, pancreatic tail, and splenic flexure of the colon were firmly attached to one another. Splenectomy combined with resection of the distal pancreas and splenic flexure of the colon was performed. In the distal pancreatectomy specimen, a 0.8-cm solid mass was present in the tail. The tumor contained definite components of both adenocarcinoma and squamous cell carcinoma. The patient died of cachexia five months after admission. This case is unique in that the metastatic tumor involving the spleen was considerably larger than the primary tumor itself.

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[304]

TÍTULO / TITLE: - Solid pseudopapillary pancreatic tumor as a portal hypertension causal: the first reported case in Puerto Rico.

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

REVISTA / JOURNAL: - Bol Asoc Med P R. 2013;105(2):54-8.

AUTORES / AUTHORS: - Torres-Miranda D; Garcia-Gubern C; Santiago M; Sanchez-Gaetan F

INSTITUCIÓN / INSTITUTION: - Ponce School of Medicine and Health Sciences, Ponce, Puerto Rico. darcy237@hotmail.com

RESUMEN / SUMMARY: - We describe the first reported case in Puerto Rico of Solid Pseudopapillary Tumor (SPT) of the pancreas causing portal hypertension. Clinical presentation and characteristic imaging findings are helpful to differentiate SPT from pancreatic carcinoma. Diagnosis can be confirmed by histopathological and immunohistochemical approach through biopsy. Timely surgical intervention can prevent portal hypertension as manifestation and be lifesaving in case of malignant degeneration, giving the patient an excellent prognosis after tumor surgical resection.

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[305]

TÍTULO / TITLE: - Diagnostic utility of endoscopic ultrasound guided aspiration cytology in evaluation of pancreatic masses.

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

REVISTA / JOURNAL: - J Coll Physicians Surg Pak. 2013 Jul;23(7):484-6. doi: 07.2013/JCPSP.484486.

AUTORES / AUTHORS: - Qureshi A; Hassan U; Loya A; Akhter N; Najam-Ud-Din; Yusuf A

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Sultan Qaboos University Hospital, Muscat, Oman.

RESUMEN / SUMMARY: - Objective: To determine the sensitivity and specificity of endoscopic ultrasound (EUS) guided fine needle aspiration cytology (FNAC) in the evaluation of pancreatic masses. Study Design: Analytical study. Place and Duration of Study: Department of Pathology, Shaukat Khanum Cancer Hospital and Research Centre, from January 2006 to June 2011. Methodology: Patients of either gender aged above 18 years who underwent EUS guided FNAC of pancreatic masses detected on abdominal CT, were included in the study. Biphasic abdominal CT scans were carried out for all the patients, followed by EUS guided FNAC. All material aspirated for cytologic evaluation was assessed for sample adequacy on-site, followed by formal examination for diagnostic purposes. Results: The mean age of patients tested was 58.94 +/- 12.84 years with age ranging from 23 to 78 years. Regarding gender 23/42 (54.76%) patients were male and 19/42 (45.24%) were female. Out of 42 cases, 27 (64%) cases were diagnosed as adenocarcinoma, 4 (9.5%) as benign, 4 (9.5%) as mucinous cystic neoplasm, 2 (4.7%) as chronic pancreatitis, 2 (4.7%) as non-diagnostic, 2 (4.7%) as atypical cells seen and 1 (2.38%) as non-Hodgkin's lymphoma. The results were in full concordance with radiologic findings. Conclusion: EUS guided FNA is an excellent procedure for evaluation of pancreatic masses. The overall sensitivity of this procedure is 89% and the specificity is 67%.

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[306]

TÍTULO / TITLE: - Maximal daily dose of pancreatic enzyme replacement therapy in infants with cystic fibrosis: A reconsideration.

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

REVISTA / JOURNAL: - J Cyst Fibros. 2013 Jun 26. pii: S1569-1993(13)00102-1. doi: 10.1016/j.jcf.2013.05.011.

●● Enlace al texto completo (gratuito o de pago) 1016/j.jcf.2013.05.011

AUTORES / AUTHORS: - Borowitz D; Gelfond D; Maguiness K; Heubi JE; Ramsey B

INSTITUCIÓN / INSTITUTION: - State University of New York at Buffalo School of Medicine and Biomedical Sciences, Department of Pediatrics, Women and Children's Hospital of Buffalo, Buffalo, NY, United States. Electronic address: dborowitz@upa.chob.edu.

RESUMEN / SUMMARY: - The current recommendations for dosing of pancreatic enzyme replacement therapy (PERT) in infants with cystic fibrosis (CF) were made using a limited evidence base. The per meal recommended dose was extrapolated from dosing guidelines for older patients into a maximal daily dose for infants. We discuss why this maximal daily dose recommendation may be insufficient for young infants with CF, although the optimal dose of PERT for infants with CF remains unknown.

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[307]

TÍTULO / TITLE: - SmacN7 enhances the sensitivity of pancreatic cancer cells to tumor necrosis factor-related apoptosis-inducing ligand or gemcitabine.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Oncol Lett. 2013 Jun;5(6):1760-1764. Epub 2013 Apr 3.
●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1285
AUTORES / AUTHORS: - Zhou W; Shi J; Niu Z; Luo H; Tian H; Gao J; Yu F; Li S
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Shandong Cancer Hospital, Jinan 250017;
RESUMEN / SUMMARY: - The aim of this study was to investigate the effect of SmacN7 on the biological characteristics of pancreatic cancer cell lines, and to assess the effect of SmacN7 on the sensitivity to tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL) and gemcitabine. SmacN7 fusion polypeptide was synthesized and characterized using mass spectrometry. The morphology of apoptotic SW1990 cells and apoptotic rates were observed after 24 h of SmacN7 treatment, and the changes of cell growth inhibition rate were investigated following treatment with different concentrations of SmacN7. The combined effects of SmacN7 and different concentrations of TRAIL or gemcitabine for 24 h on the apoptotic rates of SW1990 cells were assessed, and the changes of expression of apoptosis-related proteins including X-linked inhibitor of apoptosis protein (XIAP), cytochrome C and caspase-3 were determined. Mass spectrometric identification of SmacN7 was fully consistent with the expected results. The cell growth inhibition rates of SW1990 cells 24 h post-treatment with TRAIL at different concentrations were 18.11, 37.67, 42.63 and 67.6%, in comparison to 17.65, 31.85, 40.11 and 74.99% following combined treatment of SmacN7 and different concentrations of gemcitabine for 24 h. The combined treatment of SmacN7 and gemcitabine for 24 h resulted in significantly elevated expression of cytochrome C and caspase-3 cleavage fragment, p17, and a significant reduction in XIAP expression ($P<0.05$). SmacN7 inhibits pancreatic cell growth. The inhibition rates of SW1990 cells caused by treatment with various concentrations of SmacN7 appear in a time- and concentration-dependent manner. The TRAIL- or gemcitabine-induced apoptosis of pancreatic cancer cells, enhanced by SmacN7, may be associated with the activity of intracellular pro-apoptotic proteins such as Smac/DIABLO (second mitochondria-derived activator of caspase/direct IAP binding protein with low PI), cytochrome C, XIAP and caspase-3.

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[308]
TÍTULO / TITLE: - Pancreatic Cancer Genomes: Toward Molecular Subtyping and Novel Approaches to Diagnosis and Therapy.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Mol Diagn Ther. 2013 Jun 12.
●● Enlace al texto completo (gratuito o de pago) 1007/s40291-013-0043-6
AUTORES / AUTHORS: - Wood LD

INSTITUCIÓN / INSTITUTION: - Department of Pathology, The Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins University School of Medicine, Weinberg 2242, 401 North Broadway, Baltimore, MD, 21231, USA, ldwood@jhmi.edu.

RESUMEN / SUMMARY: - Pancreatic neoplasms represent a broad range of clinical entities, many of which have drastic effects on the lives of patients. Recently, high-throughput sequencing analyses have been performed in many pancreatic neoplasms, providing deep insights into the underlying biology of these neoplasms as well as novel approaches to diagnosis and treatment. This review discusses the molecular alterations underlying pancreatic neoplasms as well as the clinical impact of these alterations for diagnosis and treatment.

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[309]

TÍTULO / TITLE: - Endoscopic ultrasound-guided hepaticogastrostomy for advanced cholangiocarcinoma after failed stenting by endoscopic retrograde cholangiopancreatography.

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

REVISTA / JOURNAL: - Asian J Surg. 2013 Jun 12. pii: S1015-9584(13)00036-5. doi: 10.1016/j.asjsur.2013.04.007.

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

1016/j.asjsur.2013.04.007

AUTORES / AUTHORS: - Panpimanmas S; Ratanachu-Ek T

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok 10400, Thailand. Electronic address: sukijpan@hotmail.com.

RESUMEN / SUMMARY: - OBJECTIVE: Cholangiocarcinoma is common in Thailand. There are many palliative treatments available for patients with unresectable tumor, such as endoscopic retrograde cholangiopancreatography (ERCP) with stents, percutaneous transhepatic biliary drainage, or surgery. In cases in which ERCP has failed, we propose an alternative technique: the use of endoscopic ultrasound with fluoroscopy to perform hepaticogastrostomy for palliative drainage instead of percutaneous transhepatic biliary drainage. PATIENTS AND METHODS: A case series study was conducted between December 2005 and December 2009 of 10 patients (4 male and 6 female, average age: 57 years) who presented with severe jaundice caused by advanced cholangiocarcinoma, who were treated with this procedure after failure to drain by ERCP. We used an electronic convex curved linear-array fluoroscopy-guided echoendoscope to drain the left dilated intrahepatic duct to the stomach by metallic wallstent. We performed the procedure with the first six patients under general anesthesia and with the other four under conscious sedation. Follow-up liver function tests were done, and clinical symptoms and survival times were recorded. RESULTS: Hepaticogastrostomy was unsuccessful on the first two patients (success rate = 8/10; 80%), and effective drainage was obtained in only seven patients. Average total bilirubin reduction

was 14.96 mg/dL (58.75%) and 18.13 mg/dL (71.20%) after 2 weeks and 4 weeks, respectively, with good quality of life. One patient was not effectively drained because of malposition of the stent. There were two patients whose stent migrated into the stomach; one needed a second session with a second wallstent, and the other needed a double pigtail stent inside the second wallstent. Follow-up survival rates were 32-194 days (average: 123 days). CONCLUSION: Endoscopic-ultrasound-guided hepaticogastrostomy is safe and can be a good palliative option for advanced malignant biliary obstruction because it drains internally and is remote from the tumor site, promoting a long patency period of prosthesis and better quality of life.

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[310]

TÍTULO / TITLE: - Red Liriope platyphylla stimulated the insulin secretion through the regulation of calcium concentration in rat insulinoma cells and animal models.

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

REVISTA / JOURNAL: - Lab Anim Res. 2013 Jun;29(2):84-95. doi: 10.5625/lar.2013.29.2.84. Epub 2013 Jun 24.

●● Enlace al texto completo (gratuito o de pago) 5625/lar.2013.29.2.84

AUTORES / AUTHORS: - Lee HR; Kim JE; Lee YJ; Kwak MH; Im DS; Hwang DY

INSTITUCIÓN / INSTITUTION: - Department of Biomaterials Science, College of Natural Resources & Life Science, Pusan National University, Miryang, Korea.

RESUMEN / SUMMARY: - The aim of this study was to investigate the effects of Red L. platyphylla (RLP) on calcium and glucose levels during insulin secretion. To achieve this, alteration of insulin and calcium concentrations was measured in rat insulinoma-1 (INS-1) cells and animal models in response to RLP treatment. In INS-1 cells, maximum secretion of insulin was detected upon treatment with 200 microg/mL of RLP for 20 min. Nifedipine, an L-type calcium channel blocker, effectively inhibited insulin secretion from INS-1 cells. Regarding calcium levels, the maximum concentration of intracellular calcium in INS-1 cells was obtained by treatment with 100 microg/mL of RLP, whereas this level was reduced under conditions of 200 microg/mL of RLP. Further, RLP-treated INS-1 cells showed a higher level of intracellular calcium than that of L. platyphylla (LP), Korea White Ginseng (KWG), or Korea Red Ginseng (KRG)-treated cells. This RLP-induced increase in intracellular calcium was abrogated but not completely abolished upon treatment with 40 microM nifedipine in a dose-dependent manner. Furthermore, the insulin level was dramatically elevated upon co-treatment with high concentrations of glucose and RLP, whereas it was maintained at a low level in response to glucose and RLP co-treatment at low concentrations. In an animal experiment, the serum concentration of calcium increased or decreased upon RLP treatment according to glucose level compared to vehicle treatment. Therefore, these results suggest that insulin secretion induced by RLP treatment may be tightly

correlated with calcium regulation, which suggests RLP is an excellent candidate for diabetes treatment.

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[311]

TÍTULO / TITLE: - Involvement of endoplasmic reticulum stress in capsaicin-induced apoptosis of human pancreatic cancer cells.

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

REVISTA / JOURNAL: - Evid Based Complement Alternat Med. 2013;2013:629750. doi: 10.1155/2013/629750. Epub 2013 May 28.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/629750

AUTORES / AUTHORS: - Lin S; Zhang J; Chen H; Chen K; Lai F; Luo J; Wang Z; Bu H; Zhang R; Li H; Tong H

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang 310003, China ; Department of Hepatobiliary-Pancreatic Surgery, The Second Affiliated Hospital of Wenzhou Medical College, Wenzhou, Zhejiang 325027, China.

RESUMEN / SUMMARY: - Capsaicin, main pungent ingredient of hot chilli peppers, has been shown to have anticarcinogenic effect on various cancer cells through multiple mechanisms. In this study, we investigated the apoptotic effect of capsaicin on human pancreatic cancer cells in both in vitro and in vivo systems, as well as the possible mechanisms involved. In vitro, treatment of both the pancreatic cancer cells (PANC-1 and SW1990) with capsaicin resulted in cells growth inhibition, G0/G1 phase arrest, and apoptosis in a dose-dependent manner. Knockdown of growth arrest- and DNA damage-inducible gene 153 (GADD153), a marker of the endoplasmic-reticulum-stress- (ERS-) mediated apoptosis pathway, by specific siRNA attenuated capsaicin-induced apoptosis both in PANC-1 and SW1990 cells. Moreover, in vivo studies capsaicin effectively inhibited the growth and metabolism of pancreatic cancer and prolonged the survival time of pancreatic cancer xenograft tumor-induced mice. Furthermore, capsaicin increased the expression of some key ERS markers, including glucose-regulated protein 78 (GRP78), phosphoprotein kinase-like endoplasmic reticulum kinase (phosphoPERK), and phosphoeukaryotic initiation factor-2 alpha (phospho-eIF2 alpha), activating transcription factor 4 (ATF4) and GADD153 in tumor tissues. In conclusion, we for the first time provide important evidence to support the involvement of ERS in the induction of apoptosis in pancreatic cancer cells by capsaicin.

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[312]

TÍTULO / TITLE: - Spiclomazine induces apoptosis associated with the suppression of cell viability, migration and invasion in pancreatic carcinoma cells.

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

REVISTA / JOURNAL: - PLoS One. 2013 Jun 20;8(6):e66362. doi: 10.1371/journal.pone.0066362. Print 2013.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0066362

AUTORES / AUTHORS: - Zhao W; Li D; Liu Z; Zheng X; Wang J; Wang E

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Electroanalytical Chemistry, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun, Jilin, China.

RESUMEN / SUMMARY: - The effective treatment for pancreatic carcinoma remains critically needed. Herein, this current study showed that spiclomazine treatment caused a reduction in viability in pancreatic carcinoma cell lines CFPAC-1 and MIA PaCa-2 in vitro. It was notable in this regard that, compared with pancreatic carcinoma cells, normal human embryonic kidney (HEK-293) and liver (HL-7702) cells were more resistant to the antigrowth effect of spiclomazine. Biochemically, spiclomazine treatment regulated the expression of protein levels in the apoptosis related pathways. Consistent with this effect, spiclomazine reduced the mitochondria membrane potential, elevated reactive oxygen species, and activated caspase-3/9. In addition, a key finding from this study was that spiclomazine suppressed migration and invasion of cancer cells through down-regulation of MMP-2/9. Collectively, the proposed studies did shed light on the antiproliferation effect of spiclomazine on pancreatic carcinoma cell lines, and further clarified the mechanisms that spiclomazine induced apoptosis associated with the suppression of migration and invasion.

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[313]

TÍTULO / TITLE: - A case of inoperable malignant insulinoma with resistant hypoglycemia who experienced the most significant clinical improvement with everolimus.

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

REVISTA / JOURNAL: - Case Rep Endocrinol. 2013;2013:636175. doi: 10.1155/2013/636175. Epub 2013 May 8.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/636175

AUTORES / AUTHORS: - Bozkirli E; Bakiner O; Abali H; Andic C; Yapar AF; Kayaselcuk F; Ertorer E

INSTITUCIÓN / INSTITUTION: - Division of Endocrinology and Metabolism, Adana Medical Center, Baskent University School of Medicine, Dadaloglu Mah. Serin Evler 39, Sok. No. 6 Yuregir, 01250 Adana, Turkey.

RESUMEN / SUMMARY: - Metastatic insulinomas may sometimes present with recurrent life-threatening hypoglycemia episodes. Such patients usually fail to respond to various therapeutic agents which causes constant dextrose infusion requirement. Herein, we present a resistant case of inoperable malignant insulinoma who was treated with many therapeutic agents and interventions including somatostatin analogues, Yttrium-90 radioembolization, everolimus, radiotherapy, and chemoembolization. Close blood sugar monitorization during

these therapies showed the most favourable response with everolimus. Everolimus treatment resulted in rapid improvement of hypoglycemia episodes, letting us discontinue dextrose infusion and discharge the patient. However, experience with everolimus in such patients is still limited, and more precise data can be obtained with the increasing use of this agent for neuroendocrine tumours.

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[314]

TÍTULO / TITLE: - Incidence and trends of malignant and benign pancreatic lesions in Yazd, Iran between 2001 and 2011.

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

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(4):2631-5.

AUTORES / AUTHORS: - Zahir ST; Arjmand A; Kargar S; Neishaboury M

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Taghipour@ssu.ac.ir

RESUMEN / SUMMARY: - BACKGROUND: Despite recent valuable steps in initiating a cancer registry in Iran, data depicting prevalence, incidence, and clinical picture of pancreatic tumors in the country are exceedinglyly sparse. With the aim of filling this knowledge gap, we reviewed cases in the pathology archive of Shahid Sadoughi hospital (Yazd, Iran), between 2001 and 2011. MATERIALS AND METHODS: Medical records of 177 patients are reported in the present study. In cases for which paraffin-embedded blocks were available, the specimens were evaluated by two independent pathologists blinded to the primary diagnosis. We extrapolated the frequency of malignant lesions in our study to the population of Yazd province, derived from national census data, to generate cancer incidence rates. RESULTS: Final diagnosis of malignancy was made in 117 cases (66.1%), and the remainder (60 lesions, 33.9%) were classified as benign. Adenecarcinoma and neuroendocrine tumors were the two most common histological types of malignancy identified in 88 (75.2%) and 11 (9.4%) specimens, respectively. Crude annual incidence of pancreatic cancer was 0.55 per 100,000 person in 2001 and increased to 1.68 in 2011. Age standardized incidence rates in 2001 and 2011 were 0.75 and 2.68, respectively. A significant increasing trend in cancer incidence was observed during the 11 years of the study period (r =+0.856, p=0.009). Sex-stratified analysis, confirmed the observed trend in men (r=+0.728, p=0.034), but not women (r=+0.635, p=0.083). CONCLUSIONS: Over the past decade, incidence of pancreas malignancies has risen steadily in Yazd, Iran. Nevertheless, these figures are still substantially lower than those prevalent in developed nations.

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[315]

TÍTULO / TITLE: - A foregut cystic neoplasm with diagnostic and therapeutic similarities to mucinous cystic neoplasms of the pancreas.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):446-9. doi: 10.6092/1590-8577/1402.

AUTORES / AUTHORS: - Kluger MD; Tayar C; Belli A; Salceda JA; Van Nhieu JT; Luciani A; Cherqui D

INSTITUCIÓN / INSTITUTION: - Hepatobiliary Surgery and Liver Transplantation, Weill Cornell Medical College. New York, NY, USA. mik9020@med.cornell.edu.

RESUMEN / SUMMARY: - CONTEXT: Greater utilization of cross-sectional abdominal imaging has increased the diagnostic frequency of cystic neoplasms of the pancreas. The “International Consensus Guidelines 2012 for the Management of IPMN and MCN of the Pancreas” illustrates a diagnostic and therapeutic algorithm for these lesions based on current knowledge. CASE REPORT: We present a case of a 49-year-old woman with two years of intermittent epigastric pain found to have an 8.5 cm head of the pancreas mass on CT. Evaluation was consistent with a mucinous cystic neoplasm for which she underwent an uneventful pancreaticoduodenectomy. Histology revealed a bronchogenic cyst of the head of the pancreas. DISCUSSION: Bronchogenic cysts are congenital anomalies of the ventral foregut that can migrate into the abdomen prior to fusion of the diaphragm. They can easily be misdiagnosed for other benign and malignant retroperitoneal lesions. Similarly to mucinous cystic neoplasms, bronchogenic cysts have been reported to undergo malignant transformation. They can also become infected and hemorrhage. Therefore, resection should be performed in appropriate risk candidates. It is possible, with increased use of high resolution cross-sectional imaging, that these lesions may be identified with greater frequency in the abdomen and confused with other pancreatic neoplasms. The presence of ciliated respiratory epithelium and cartilage on pathology provides for definitive diagnosis.

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[316]

TÍTULO / TITLE: - Mesothelin Virus-Like Particle Immunization Controls Pancreatic Cancer Growth through CD8(+) T Cell Induction and Reduction in the Frequency of CD4(+)foxp3(+)ICOS(-) Regulatory T Cells.

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

REVISTA / JOURNAL: - PLoS One. 2013 Jul 9;8(7):e68303. doi: 10.1371/journal.pone.0068303. Print 2013.

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

1371/journal.pone.0068303

AUTORES / AUTHORS: - Zhang S; Yong LK; Li D; Cubas R; Chen C; Yao Q

INSTITUCIÓN / INSTITUTION: - Molecular Surgeon Research Center, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Texas, United States of America.

RESUMEN / SUMMARY: - Our previous study has shown that mesothelin (MSLN) is a potential immunotherapeutic target for pancreatic cancer. Here, we further studied the immunogenicity of chimeric murine MSLN-virus-like particles (mMSLN-VLPs), their ability to break tolerance to mMSLN, a self-antigen, and deciphered the mechanism of immune responses elicited by mMSLN-VLP immunization using a pancreatic cancer (PC) mouse model. In addition to what we have found with xenogeneic human MSLN-VLP (hMSLN-VLP), mMSLN-VLP immunization was able to break the tolerance to intrinsic MSLN and mount mMSLN-specific, cytotoxic CD8(+) T cells which led to a significant reduction in tumor volume and prolonged survival in an orthotopic PC mouse model. Furthermore, CD4(+)foxp3(+) regulatory T cells (Tregs) were progressively decreased in both spleen and tumor tissues following mMSLN-VLP immunization and this was at least partly due to elevated levels of IL-6 production from activated plasmocytoid dendritic cell (pDC)-like cells following mMSLN-VLP immunization. Moreover, mMSLN-VLP treatment mainly reduced the frequency of the CD4(+)foxp3(+)ICOS(-) Treg subset. However, mMSLN-VLP induced IL-6 production also increased ICOSL expression on pDC-like cells which supported the proliferation of immunosuppressive CD4(+)foxp3(+)ICOS(+) Treg cells. This study reveals that mMSLN-VLP immunization is capable of controlling PC progression by effectively mounting an immune response against mMSLN, a tumor self-antigen, and altering the immunosuppressive tumor microenvironment via activation of pDCs-like cells and reduction in the frequency of CD4(+)foxp3(+)ICOS(-) Treg cells. However, combination therapies will likely need to be used in order to target residual CD4(+)foxp3(+)ICOS(+) Treg cells.

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[317]

TÍTULO / TITLE: - Cercariform cells: another cytologic feature distinguishing solid pseudopapillary neoplasms from pancreatic endocrine neoplasms and acinar cell carcinomas in endoscopic ultrasound-guided fine-needle aspirates.

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

REVISTA / JOURNAL: - Cancer Cytopathol. 2013 Jun;121(6):298-310. doi: 10.1002/cncy.21259. Epub 2012 Dec 5.

●● Enlace al texto completo (gratuito o de pago) 1002/cncy.21259

AUTORES / AUTHORS: - Samad A; Shah AA; Stelow EB; Alsharif M; Cameron SE; Pambuccian SE

INSTITUCIÓN / INSTITUTION: - Department of Laboratory Medicine and Pathology, University of Minnesota, University of Minnesota Medical Center, Fairview, Minneapolis, Minnesota, USA.

RESUMEN / SUMMARY: - BACKGROUND: Solid pseudopapillary neoplasm (SPPN) is a rare tumor of unknown origin that occurs predominantly in the body or tail of the pancreas in young women. The authors recently identified cercariform (Greek: tailed) cells, similar to those described in urothelial carcinomas, as a consistent cytologic feature in ultrasound-guided fine-needle

aspiration (EUS-FNA) samples from SPPNs. The objective of the current multi-institutional study was to define the value of these cells in the differential diagnosis of SPPN with other neoplasms characterized cytologically by the presence of monotonous, uniform cells in pancreatic aspirates: pancreatic neuroendocrine tumors (Pan-NETs) and acinar cell carcinomas (ACCs). METHODS: The files of 4 academic hospitals were searched for SPPNs, Pan-NETs, and ACCs that were diagnosed by EUS-FNA. The slides were reviewed, and several cytologic features were recorded semiquantitatively to identify discriminating features between SPPNs, Pan-NETs, and ACCs. RESULTS: From the analysis of 18 SPPNs, 4 ACCs, and 20 Pan-NETs, the following cytologic features were identified as common to all 3 neoplasms: single cells and rosettes/acinar cell groups, round-to-plasmacytoid cells, pale-to-granular cytoplasm, fine vacuoles, and binucleated cells. Papillary structures, cercariform cells, large cytoplasmic vacuoles, reniform nuclei, hyaline globules/magenta-colored material, and degenerative features (cholesterol crystals, calcifications, foam cells, or giant cells) were significantly more common in SPPNs. Prominent nuclear grooves were encountered in only 4 of 18 SPPNs. CONCLUSIONS: The current results indicated that the presence of cercariform cells is another useful clue for the cytologic diagnosis of SPPN in challenging cases.

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[318]

TÍTULO / TITLE: - Cannabinoids inhibit energetic metabolism and induce AMPK-dependent autophagy in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Cell Death Dis. 2013 Jun 13;4:e664. doi: 10.1038/cddis.2013.151.

●● Enlace al texto completo (gratuito o de pago) 1038/cddis.2013.151

AUTORES / AUTHORS: - Dando I; Donadelli M; Costanzo C; Dalla Pozza E; D'Alessandro A; Zolla L; Palmieri M

INSTITUCIÓN / INSTITUTION: - Department of Life and Reproduction Sciences, Biochemistry Section, University of Verona, Verona, Italy.

RESUMEN / SUMMARY: - The anti-tumoral effects of cannabinoids have been described in different tumor systems, including pancreatic adenocarcinoma, but their mechanism of action remains unclear. We used cannabinoids specific for the CB1 (ACPA) and CB2 (GW) receptors and metabolomic analyses to unravel the potential pathways mediating cannabinoid-dependent inhibition of pancreatic cancer cell growth. Panc1 cells treated with cannabinoids show elevated AMPK activation induced by a ROS-dependent increase of AMP/ATP ratio. ROS promote nuclear translocation of GAPDH, which is further amplified by AMPK, thereby attenuating glycolysis. Furthermore, ROS determine the accumulation of NADH, suggestive of a blockage in the respiratory chain, which in turn inhibits the Krebs cycle. Concomitantly, inhibition of Akt/c-Myc pathway leads to decreased activity of both the pyruvate kinase isoform M2 (PKM2), further downregulating glycolysis, and glutamine uptake. Altogether,

these alterations of pancreatic cancer cell metabolism mediated by cannabinoids result in a strong induction of autophagy and in the inhibition of cell growth.

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[319]

TÍTULO / TITLE: - Endosonography-assisted transmural endoscopic drainage of pancreatic pseudocysts: A single center experience.

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

REVISTA / JOURNAL: - Turk J Gastroenterol. 2012 Dec;23(6):741-6.

AUTORES / AUTHORS: - Sisman G; Gurcu B; Unalp O; Yilmaz F; Nart D; Sozbilen M; Coker A

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Istanbul University, Cerrahpasa School of Medicine, Istanbul.

RESUMEN / SUMMARY: - Background/aims:Identification of the predictive factors for the prognosis of gastroenteropancreatic neuroendocrine tumors is important but rather challenging due to the rarity of the condition. This study aimed to examine the association between somatostatin receptor-2 positivity and known prognostic factors for gastroenteropancreatic neuroendocrine tumor to identify the value ofsomatostatin receptor-2 positivity itself as a predictive factor for prognosis. Materials and Methods: Records of 41 gastroenteropancreatic neuroendocrine tumor patients (24 females, 17 males) were retrospectively reviewed. The relations between somatostatin eceptor-2 positivity and known prognostic factors including tumor stage, Ki-67 positivity, vascular or perineural invasion, lymph node metastasis, presence of necrosis, and soft tissue extension were analyzed. Results:Sixty percent of the patients had histologically confirmed somatostatin receptor-2 positivity with 45% exhibiting focal and 15% showing diffuse staining characteristic. No significant relation was found between somatostatin receptor-2 positivity and any of the known prognostic factors for gastroenteropancreatic neuroendocrine tumor: versus stage, p=0.67; vs. lymph node metastasis, p=0.51; vs. vascular invasion, p=0.11; vs. extension to surrounding soft tissue, p=0.54; vs. necrosis, p=0.23; vs. lymphatic invasion, p=0.25; and vs. perineural invasion, p=0.42. Conclusions:Somatostatin receptor-2 positivity, either focal or diffuse, does not seem to predict prognosis in gastroenteropancreatic neuroendocrine tumors. However, growing evidence supports the benefits of somatostatin analogues as adjunctive treatment in this group of patients.

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[320]

TÍTULO / TITLE: - The cancer-associated FGFR4-G388R polymorphism enhances pancreatic insulin secretion and modifies the risk of diabetes.

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

REVISTA / JOURNAL: - Cell Metab. 2013 Jun 4;17(6):929-40. doi: 10.1016/j.cmet.2013.05.002.

●● Enlace al texto completo (gratuito o de pago)
1016/j.cmet.2013.05.002
AUTORES / AUTHORS: - Ezzat S; Zheng L; Florez JC; Stefan N; Mayr T; Hliang MM; Jablonski K; Harden M; Stancakova A; Laakso M; Haring HU; Ullrich A; Asa SL
INSTITUCIÓN / INSTITUTION: - Ontario Cancer Institute, University Health Network, Toronto, ON M5G 2M9, Canada. shereen.ezzat@utoronto.ca
RESUMEN / SUMMARY: - The fibroblast growth factor receptor 4 (FGFR4)-R388 single-nucleotide polymorphism has been associated with cancer risk and prognosis. Here we show that the FGFR4-R388 allele yields a receptor variant that preferentially promotes STAT3/5 signaling. This STAT activation transcriptionally induces Grb14 in pancreatic endocrine cells to promote insulin secretion. Knockin mice with the FGFR4 variant allele develop pancreatic islets that secrete more insulin, a feature that is reversed through Grb14 deletion and enhanced with FGF19 administration. We also show in humans that the FGFR4-R388 allele enhances islet function and may protect against type 2 diabetes. These data support a common genetic link underlying cancer and hyperinsulinemia.

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[321]
TÍTULO / TITLE: - Serous cystadenocarcinoma of pancreas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - J Coll Physicians Surg Pak. 2013 Jun;23(6):430-1. doi: 06.2013/JCPSP.430431.
AUTORES / AUTHORS: - Rathore MU; Arif A; Umair B
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Combined Military Hospital, Quetta. usmanrathore78@gmail.com
RESUMEN / SUMMARY: - Serous cystic neoplasms of pancreas are relatively rare tumours. Malignancy in these tumours is even more rare which is confirmed by metastasis to other organs or by perineural, vascular or surrounding soft tissue invasion. A 60 years old lady presented with vague upper abdominal pain. Computed tomography scan showed multiloculated cystic mass in the body of pancreas measuring 9 x 6 x 5 cm and not involving spleen. Pancreatectomy specimen showed a multicystic tumour having sponge-like appearance which showed vascular and soft tissue invasion of surrounding stroma on microscopic examination and was diagnosed as serous cystadenocarcinoma of pancreas.

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[322]
TÍTULO / TITLE: - Galectin-4 Reduces Migration and Metastasis Formation of Pancreatic Cancer Cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - PLoS One. 2013 Jun 18;8(6):e65957. Print 2013.

●● Enlace al texto completo (gratuito o de pago)
1371/journal.pone.0065957
AUTORES / AUTHORS: - Belo AI; van der Sar AM; Tefsen B; van Die I
INSTITUCIÓN / INSTITUTION: - Department of Molecular Cell Biology and Immunology, VU University Medical Centre, Amsterdam, The Netherlands.
RESUMEN / SUMMARY: - Galectin-4 (Gal-4) is a member of the galectin family of glycan binding proteins that shows a significantly higher expression in cystic tumors of the human pancreas and in pancreatic adenocarcinomas compared to normal pancreas. However, the putative function of Gal-4 in tumor progression of pancreatic cancer is still incompletely understood. In this study the role of Gal-4 in cancer progression was investigated, using a set of defined pancreatic cancer cell lines, Pa-Tu-8988S (PaTu-S) and Pa-Tu-8988T (PaTu-T), as a model. These two cell lines are derived from the same liver metastasis of a human primary pancreatic adenocarcinoma, but differ in their growth characteristics and metastatic capacity. We demonstrated that Gal-4 expression is high in PaTu-S, which shows poor migratory properties, whereas much lower Gal-4 levels are observed in the highly metastatic cell line PaTu-T. In PaTu-S, Gal-4 is found in the cytoplasm, but it is also secreted and accumulates at the membrane at sites of contact with neighboring cells. Moreover, we show that Gal-4 inhibits metastasis formation by delaying migration of pancreatic cancer cells in vitro using a scratch assay, and in vivo using zebrafish (Danio rerio) as an experimental model. Our data suggest that Gal-4 may act at the cell-surface of PaTu-S as an adhesion molecule to prevent release of the tumor cells, but has in addition a cytosolic function by inhibiting migration via a yet unknown mechanism.

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[323]
TÍTULO / TITLE: - Gossypol and an HMT G9a inhibitor act in synergy to induce cell death in pancreatic cancer cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cell Death Dis. 2013 Jun 27;4:e690. doi: 10.1038/cddis.2013.191.
●● Enlace al texto completo (gratuito o de pago) 1038/cddis.2013.191
AUTORES / AUTHORS: - Yuan Y; Tang AJ; Castoreno AB; Kuo SY; Wang Q; Kuballa P; Xavier R; Shamji AF; Schreiber SL; Wagner BK
INSTITUCIÓN / INSTITUTION: - 1] Chemical Biology Program, Broad Institute, Cambridge, MA, USA [2] Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, USA.
RESUMEN / SUMMARY: - The histone methyltransferase G9a is overexpressed in a variety of cancer types, including pancreatic adenocarcinoma, and promotes tumor invasiveness and metastasis. We recently reported the discovery of BRD4770, a small-molecule inhibitor of G9a that induces senescence in PANC-1 cells. We observed that the cytotoxic effects of BRD4770 were dependent on genetic background, with cell lines lacking functional p53 being relatively

resistant to compound treatment. To understand the mechanism of genetic selectivity, we used two complementary screening approaches to identify enhancers of BRD4770. The natural product and putative BH3 mimetic gossypol enhanced the cytotoxicity of BRD4770 in a synergistic manner in p53-mutant PANC-1 cells but not in immortalized non-tumorigenic pancreatic cells. The combination of gossypol and BRD4770 increased LC3-II levels and the autophagosome number in PANC-1 cells, and the compound combination appears to act in a BNIP3 (B-cell lymphoma 2 19-kDa interacting protein)-dependent manner, suggesting that these compounds act together to induce autophagy-related cell death in pancreatic cancer cells.

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[324]

TÍTULO / TITLE: - Drug-eluting scaffold to deliver chemotherapeutic medication for management of pancreatic cancer after surgery.

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

REVISTA / JOURNAL: - Int J Nanomedicine. 2013;8:2465-72. doi: 10.2147/IJN.S47666. Epub 2013 Jul 11.

●● Enlace al texto completo (gratuito o de pago) 2147/IJN.S47666

AUTORES / AUTHORS: - Zhan Q; Shen B; Deng X; Chen H; Jin J; Zhang X; Peng C; Li H

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Rui Jin Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, People's Republic of China.

RESUMEN / SUMMARY: - Traditional post-surgical chemotherapy for pancreatic cancer is notorious for its devastating side effects due to the high dosage required. On the other hand, legitimate concerns have been raised about nanoparticle-mediated drug delivery because of its potential cytotoxicity. Therefore, we explored the local delivery of a reduced dosage of FOLFIRINOX, a four-drug regimen comprising oxaliplatin, leucovorin, irinotecan, and fluorouracil, for pancreatic cancer using a biocompatible drug-eluting scaffold as a novel chemotherapy strategy after palliative surgery. In vitro assays showed that FOLFIRINOX in the scaffold caused massive apoptosis and thereby a decrease in the viability of pancreatic cancer cells, confirming the chemotherapeutic capability of the drug-eluting scaffold. In vivo studies in an orthotopic murine xenograft model demonstrated that the FOLFIRINOX in the scaffold had antitumorigenic and antimetastatic effects comparable with those achieved by intraperitoneal injection, despite the dose released by the scaffold being roughly two thirds lower. A mechanistic study attributed our results to the excellent ability of the FOLFIRINOX in the scaffold to destroy the CD133(+)CXCR4(+) cell population responsible for pancreatic tumorigenesis and metastasis. This clinically oriented study gives rise to a promising alternative strategy for postsurgical management of pancreatic cancer, featuring a local chemotherapeutic effect with considerable attenuation of side effects.

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[325]

TÍTULO / TITLE: - Treatment of poorly differentiated neuroendocrine carcinoma of the pancreas.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):381-3. doi: 10.6092/1590-8577/1661.

AUTORES / AUTHORS: - Gupta A; Duque M; Saif MW

INSTITUCIÓN / INSTITUTION: - Tufts University School of Medicine. Boston, MA, USA. agupta1@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - Poorly differentiated neuroendocrine carcinoma is a rare malignancy that remains a challenge to treat. Poorly differentiated neuroendocrine carcinoma occurs at an incidence of 2% annually in United States. The current standard of care is based largely upon retrospective data. There remains a need for large prospective cooperative group trials in the management of poorly differentiated neuroendocrine carcinoma. In this paper, we will review abstract #e15096 (Paclitaxel, carboplatin, and etoposide (TCE) in advanced poorly differentiated neuroendocrine carcinoma) by Loeffler et al. and #e15071 (Poorly differentiated neuroendocrine carcinoma (NEC G3): prognostic factors and potential novel targets) by Heetfeld et al. presented at the 2013 ASCO Annual Meeting highlighting treatment options in first and second lines for poorly differentiated neuroendocrine carcinoma.

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[326]

TÍTULO / TITLE: - Pharmacogenomics in pancreatic adenocarcinoma: new data and their clinical implications.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):359-62. doi: 10.6092/1590-8577/1662.

AUTORES / AUTHORS: - Strimpakos AS; Syrigos KN; Saif MW

INSTITUCIÓN / INSTITUTION: - Tufts University School of Medicine. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - Despite advances and investments in translation research, clinical trials and health service in general, there is no significant impact on the survival of most patients diagnosed with advanced pancreatic adenocarcinoma. It is broadly recognized though that there is a small minority of patients who really benefit from particular treatments for reason usually not well understood. Light to this fact is gradually shed by developments in the field of pharmacogenomics, which plays pivotal role in what we call individualized medicine. In that perspective, it is of most importance to present the significant developments in pharmacogenomics announced in the recent 2013 American Society of Clinical Oncology Annual Meeting. First, the predictive role of hENT1, which codes for a gemcitabine transporter into cells, was highlighted and might help us decide whether we benefit from gemcitabine or 5-fluorouracil in the

adjuvant setting (Abstract #4006). Second, authors presented the negative predictive role of SPARC stroma and cytoplasmic expression in patients treated with adjuvant gemcitabine (within the CONCO-001 study) as they reported poor outcome of those having high expression, not seen in patients on observation (Abstract #4016). Finally, a study which might be a basis for future strategies and as great food for scientific thought suggested that selection of cytotoxic treatment based on gene expression profiling is feasible in clinical practice and may help improve treatment efficacy as well as predict for drug resistance (Abstract #4017). Of course, there is a long way to go before implementation of these genomic findings, with the exception of hENT1 which seems to be close for clinical use.

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[327]

TÍTULO / TITLE: - A comparison of three treatment strategies for locally advanced and borderline resectable pancreatic cancer.

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

REVISTA / JOURNAL: - J Gastrointest Oncol. 2013 Jun;4(2):123-30. doi: 10.3978/j.issn.2078-6891.2013.011.

●● Enlace al texto completo (gratuito o de pago) 3978/j.issn.2078-6891.2013.011

AUTORES / AUTHORS: - Lloyd S; Chang BW

INSTITUCIÓN / INSTITUTION: - Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT, USA.

RESUMEN / SUMMARY: - BACKGROUND: The optimal treatment strategy for locally advanced and borderline resectable pancreatic cancer is not known. We compared overall survival (OS), local control (LC), metastasis free survival (MFS), and percent of patients who were able to undergo successful surgical resection for three treatment strategies. METHODS: We retrospectively reviewed 115 sequentially treated cases of locally advanced (T4) or borderline resectable (T3 but unresectable) pancreatic cancer. Patients were treated with either chemotherapy alone ©, concurrent chemoradiation therapy (CRT), or chemotherapy followed by chemoradiation therapy (CCRT). We compared survival between groups using Kaplan-Meier analysis and Cox-proportional hazards models. RESULTS: Median follow-up was 18.7 months. Fifty-six (49%) patients had locally advanced disease. Of the patients who received chemotherapy up-front, 82/92 (89%) received gemcitabine-based chemotherapy. Of the patients receiving C alone, 11/65 (17%) were diagnosed with distant metastases or died before 3 months. The rate of successful surgical resection was 6/50 (12%) in patients treated with radiation therapy (CRT or CCRT). Median survival times for patients undergoing C, CRT, and CCRT were 13.9, 12.5, and 21.5 months respectively. Patients treated with CCRT experienced statistically significant improved OS and MFS compared to C alone (P=0.003 and P=0.012 respectively). There was no difference in LC between treatment groups. On multivariable analysis younger age (P=0.009), borderline

resectable disease (P=0.035), successful surgery (P=0.002), and receiving chemotherapy followed by chemoradiation therapy (P=0.035) were all associated with improved OS. CONCLUSIONS: Treatment with CCRT is associated with improved median OS and MFS compared with C alone. This strategy may select for patients who are less likely to develop early metastases and therefore have a better prognosis.

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[328]

TÍTULO / TITLE: - Pancreatic cancer: why is it so hard to treat?

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

REVISTA / JOURNAL: - Therap Adv Gastroenterol. 2013 Jul;6(4):321-37. doi: 10.1177/1756283X13478680.

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1177_1756283X13478680 [pii

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

1177/1756283X13478680

AUTORES / AUTHORS: - Oberstein PE; Olive KP

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Division of Hematology and Oncology, Columbia University Medical Center, New York, NY, USA.

RESUMEN / SUMMARY: - No common malignancy is as rapidly and inevitably fatal as pancreatic ductal adenocarcinoma (PDA). This grim fact has driven substantial research efforts into this disease in recent decades. Unfortunately, the investment has yet to result in a meaningful increase in 5-year survival. This has prompted many pancreatic cancer researchers and advocates to redouble their efforts, but also requires one to step back and ask why the previous efforts were lacking and to consider why pancreatic cancer is so difficult to treat. The difficulties are legion. PDA is characterized by an insidious clinical syndrome, but is rarely diagnosed at a time when surgical resection is feasible. We lack markers of early detection and screening programs remain unproven even in high risk populations. The location of the tumor in the retroperitoneum, the advanced age of patients, and the systemic effects of disease limit the options for local therapy. Chemotherapy may provide a small benefit, but most efforts to improve on the current regimens consistently and stubbornly fail in advanced clinical trials. The molecular and cellular features of ductal pancreatic tumors are aggressive and underlay multiple levels of therapeutic resistance. Non-cell-autonomous features including stromal proliferation, reduced vascular density and immune suppression also contribute to therapeutic resistance. Growing awareness of these the fundamental features of PDA has begun to guide ongoing research efforts. Clinical trials are now specifically targeting these tumor properties and actively focusing on the therapeutic implications of tumor stroma. As reviewed here, reflecting on the fundamental question of why pancreatic cancer is so difficult to treat is a necessary and informative exercise that will aid our efforts to improve patient outcomes. These efforts will lead to improvements in clinical trial design, expand our focus to include the molecular

and histologic implications of novel treatment paradigms, and ultimately change the lives of our patients.

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[329]

TÍTULO / TITLE: - Preclinical research in treatment of pancreatic cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):384-7. doi: 10.6092/1590-8577/1643.

AUTORES / AUTHORS: - Skoura E; Syrigos KN; Saif MW

INSTITUCIÓN / INSTITUTION: - Oncology Unit, Third Department of Medicine, University of Athens, Sotiria General Hospital. Athens, Greece. lskoura@yahoo.gr.

RESUMEN / SUMMARY: - Pancreatic adenocarcinoma is an aggressive type of malignancy and remains a treatment-refractory cancer. Because of the few treatment options, understanding of the molecular mechanisms is necessary, for new drugs be developed against molecular targets. Two of the novel, promising regimens against molecular targets, NVP-BEZ235 and MSK-777, were examined in three preclinical studies performed in human pancreatic cell lines and mouse models and presented in the 2013 ASCO Annual Meeting. Two of the studies evaluated the role of NVP-BEZ235, an oral phosphatidylinositol-3-kinase (PI3K) inhibitor, in pancreatic cancer treatment, alone and in combination with nab-paclitaxel (Abstract #e15007) or gemcitabine (Abstract #e15070). The third study presents the effectiveness of the novel cell division cycle 7 (Cdc7) kinase inhibitor, MSK-777 (Abstract #e15059). All studies demonstrated promising results and further investigation is ongoing.

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[330]

TÍTULO / TITLE: - Update on novel therapies for pancreatic neuroendocrine tumors: 2013.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):377-80. doi: 10.6092/1590-8577/1647.

AUTORES / AUTHORS: - Dimou A; Syrigos KN; Saif MW

INSTITUCIÓN / INSTITUTION: - Section of GI Cancers and Experimental Therapeutics, Tufts University School of Medicine. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - Neuroendocrine tumors of the pancreas (pNETs) are classified on the basis of their differentiation as well as the functional status. Current treatment options for non resectable disease include everolimus, sunitinib, somatostatin analogs and chemotherapy. A number of trials with novel compounds and drug combinations were reported at the recent ASCO Annual Meeting. Pasireotide is a novel somatostatin analog with broader affinity for the somatostatin receptors compared to the traditional octreotide and lantreotide and it appears to be safe in patients with pNETs according to a phase I study

(Abstract #e15126). The combination of octreotide with everolimus showed promising response rate and progression free survival in a phase II study (Abstract #4136). In another phase II study, the AKT inhibitor MK-2206 was well tolerated with moderate efficacy (Abstract #e15133). Last but not least, we discuss the updated data from a phase II study that used the combination of temsirolimus with bevacizumab in patients with advanced pNETs (Abstract #4032).

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[331]

TÍTULO / TITLE: - Cancer stem cell in the progression and therapy of pancreatic cancer.

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

REVISTA / JOURNAL: - Front Biosci (Landmark Ed). 2013 Jun 1;18:795-802.

AUTORES / AUTHORS: - Xu L

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Fengxian Branch of 6th Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 201400, P R China. sccdlx@126.com

RESUMEN / SUMMARY: - Pancreatic cancer (PC) is an aggressive malignancy with a high incidence of distant metastasis and mortality. Emerging evidence has demonstrated that pancreatic cancer stem cells (CSCs), which have the potential to self-renew and are pluripotent, are crucially important in the progression and therapy of PC. The origin of pancreatic CSCs was suggested to be pancreatic acinar cells, centroacinar cells, or acinar-ductal metaplasia. And several CSC-specific markers for pancreatic cancer have been reported, including CD133, CD24, CD44 and CXCR4. Several studies reported the molecular mechanisms regulating human pancreatic CSCs characteristics. In the progression of PC, CSCs are linked with the aggressiveness of PC with association of epithelial to mesenchymal transition (EMT). In the therapy of PC, especially chemotherapy, CSCs offer new insight into PC therapy, especially the mechanism of drug resistance. Therefore, strategies for modulating and treating CSCs can lead to novel targeted therapies for pancreatic cancer.

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[332]

TÍTULO / TITLE: - Inhibition of SIRT1 combined with gemcitabine therapy for pancreatic carcinoma.

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

REVISTA / JOURNAL: - Clin Interv Aging. 2013;8:889-97. doi: 10.2147/CIA.S45064. Epub 2013 Jul 16.

●● Enlace al texto completo (gratuito o de pago) 2147/CIA.S45064

AUTORES / AUTHORS: - Gong DJ; Zhang JM; Yu M; Zhuang B; Guo QQ

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary-Pancreatic Surgery, Jinhua Hospital of Zhejiang University, Jinhua, People's Republic of China.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic carcinoma possesses one of the highest lethality rates, highest drug-resistance, and highest incidence

rates. The objective of this research was to enhance the efficacy and drug-resistance for pancreatic carcinoma by using inhibition of SIRT1 combined with gemcitabine therapy methods. METHODS: Three pancreatic carcinoma cells (PANC-1 cells, BxPC-3 cells, and SW1990 cells) received treatment with physiological saline, inhibition of SIRT1, gemcitabine, and combination therapy with inhibition of SIRT1 and gemcitabine in vitro; then BxPC-3 pancreatic cancer xenogeneic mice also received treatment with physiological saline, inhibition of SIRT1, gemcitabine, and combination therapy with inhibition of SIRT1 and gemcitabine in vivo. RESULTS: The cleaved poly ADP ribose polymerase (PARP)-1 effect of drug in pancreatic carcinoma cells was significantly different ($P < 0.05$) and the efficacy in descending order was the combination therapy with inhibition of SIRT1 and gemcitabine, inhibition of SIRT1, and gemcitabine. The BxPC-3 pancreatic cancer xenogeneic mice model received treatment with physiological saline, inhibition of SIRT1, gemcitabine, and combination therapy with inhibition of SIRT1 and gemcitabine in vivo and the results showed that the tumor volumes decreased and the survival rate within 45 days increased according to the order of the given drugs and the difference was significant ($P < 0.05$). CONCLUSION: Combination therapy with inhibition of SIRT1 and gemcitabine could improve efficacy and survival time in a BxPC-3 pancreatic cancer xenogeneic mice model, compared with single inhibition of SIRT1, or single gemcitabine therapy. The combination therapy method is a potential treatment method for pancreatic carcinoma.

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[333]

TÍTULO / TITLE: - New therapeutic strategies in the second line setting of advanced or metastatic pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):344-6. doi: 10.6092/1590-8577/1650.

AUTORES / AUTHORS: - Ramfidis VS; Syrigos KN; Saif MW

INSTITUCIÓN / INSTITUTION: - Department of Medicine and Cancer Center, Tufts Medical Center. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - Pancreatic cancer is a lethal disease and its prognosis remains dismal. The modest results of existing available treatments in the second line setting reveal the need of new therapeutic strategies. In this year's American Society of Clinical Oncology (ASCO) Annual Meeting two remarkable trials and one retrospective analysis were presented regarding this vulnerable group of patients. According to the published results, docetaxel plus oxaliplatin (Abstract #4034), selumetinib plus erlotinib (Abstract #4014) and nab-paclitaxel (Abstract #e15057) have shown promising efficacy and manageable toxicity that should be elucidated and confirmed by new prospective, large, randomized trials.

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[334]

TÍTULO / TITLE: - First line therapy for metastatic pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):340-3. doi: 10.6092/1590-8577/1667.
AUTORES / AUTHORS: - Jarboe J; Saif MW
INSTITUCIÓN / INSTITUTION: - Tufts Cancer Center. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.
RESUMEN / SUMMARY: - Metastatic pancreatic cancer remains a difficult disease to treat; however, there are more new drug combinations on the horizon each week. We will discuss the results of the MPACT trial presented at the 2013 ASCO Annual Meeting (Abstracts #4005, #4058, and #4059) and compare to the 2011 FOLFIRINOX data.

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[335]
TÍTULO / TITLE: - Is s-1 a potential game changer in adjuvant therapy of pancreatic cancer?
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):329-33. doi: 10.6092/1590-8577/1640.
AUTORES / AUTHORS: - Chaulagain CP; Rothschild J; Saif MW
INSTITUCIÓN / INSTITUTION: - Division of Hematology and Oncology and Experimental Therapeutics, Tufts Medical Center and Tufts University School of Medicine. Boston, MA, USA. cchaulagain@tuftsmedicalcenter.org.
RESUMEN / SUMMARY: - There remains a lack of consensus on the optimal adjuvant therapy for pancreatic cancer. In general, chemoradiation is favored in the United States and gemcitabine based chemotherapy is favored in Europe. Both of these approaches have been shown by large prospective, randomized trials to improve disease free survivals and in some studies overall survival. We present the summary of three abstracts from the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting and discuss their potential impact on our clinical practice. Adjuvant oral chemotherapy with S-1 (Fukutomi et al., Abstract #4008) has now emerged as a promising alternative to the traditional gold standard of intravenous gemcitabine in a relatively large randomized phase III clinical trial. Another study by Yoshitomi et al. (Abstract #4056) examined the value of adjuvant chemotherapy with S-1 alone versus combination of S-1 and gemcitabine versus gemcitabine alone in a three arm phase II clinical trial (CAP-002 Study). In terms of biomarkers in pancreatic cancer, Neoptolemos et al. presented the impact of hENT1 tumor levels on the outcome of the patients with pancreatic cancer (Abstract #4006) who had received adjuvant chemotherapy with either 5-flurouracil or gemcitabine in the ESPAC trial.

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[336]
TÍTULO / TITLE: - Clinical next-generation sequencing successfully applied to fine-needle aspirations of pulmonary and pancreatic neoplasms.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cancer Cytopathol. 2013 Jul 24. doi: 10.1002/cncy.21338.

●● Enlace al texto completo (gratuito o de pago) 1002/cncy.21338

AUTORES / AUTHORS: - Young G; Wang K; He J; Otto G; Hawryluk M; Zwirco Z; Brennan T; Nahas M; Donahue A; Yelensky R; Lipson D; Sheehan CE; Boguniewicz AB; Stephens PJ; Miller VA; Ross JS

INSTITUCIÓN / INSTITUTION: - Foundation Medicine, Inc., Cambridge, Massachusetts.

RESUMEN / SUMMARY: - BACKGROUND: Next-generation sequencing was performed on pulmonary and pancreatic fine-needle aspirations (FNAs) and on paired FNAs and resected primary tumors from the same patient. METHODS: DNA was isolated in formalin-fixed, paraffin-embedded cell blocks from 16 pulmonary FNAs, 23 pancreatic FNAs, and 5 resected pancreatic primary tumors. Next-generation sequencing was performed for 4561 exons of 287 cancer-related genes and for 47 introns of 19 genes on indexed, adaptor-ligated, hybridization-captured libraries using a proprietary sequencing system (the Illumina HiSeq 2000). RESULTS: Genomic profiles were generated successfully from 16 of 16 (100%) pulmonary FNAs, which included 14 nonsmall cell lung cancers (NSCLCs) and 2 small cell lung cancers (SCLCs). The NSCLC group included 6 adenocarcinomas, 5 squamous cell carcinomas, and 3 NSCLCs not otherwise specified. Genomic profiles were successfully obtained from 23 of 23 (100%) pancreatic FNAs and from 5 of 5 (100%) matched pancreatic primary tumors, which included 17 ductal adenocarcinomas, 3 mucinous adenocarcinomas, 2 adenocarcinomas NOS, and 1 neuroendocrine tumor. Eighty-one genomic alterations were identified in the 16 pulmonary FNAs (average, 5.1 genomic alterations per patient); and the most common genomic alterations were TP53, RB1, SOX2, PIK3CA, and KRAS. Eighty-seven genomic alterations were identified in the 23 pancreatic tumor FNAs (average, 3.8 genomic alterations per patient); and the most common genomic alterations were KRAS, TP53, CDKN2A/B, SMAD4, and PTEN. Among the pancreatic tumors, there was 100% concordance of 20 genomic alterations that were identified in 5 patient-matched FNA and surgical primary tumor pairs. CONCLUSIONS: The authors were able to perform next-generation sequencing reliably on FNAs of pulmonary and pancreatic tumors, and the genomic alterations discovered correlated well with those identified in matched resected pancreatic tumors. Cancer (Cancer Cytopathol) 2013. © 2013 American Cancer Society.

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[337]

TÍTULO / TITLE: - Clinical Significance of Coagulation Assays in Metastatic Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - J Gastrointest Cancer. 2013 Jun 14.

●● Enlace al texto completo (gratuito o de pago) 1007/s12029-013-9512-8

AUTORES / AUTHORS: - Tas F; Karabulut S; Bilgin E; Kilic L; Ciftci R; Duranyildiz D

INSTITUCIÓN / INSTITUTION: - Institute of Oncology, University of Istanbul, Capa, 34390, Istanbul, Turkey, faruktas2002@yahoo.com.

RESUMEN / SUMMARY: - PURPOSE: Activated coagulation and fibrinolytic system in cancer patients is associated with tumor stroma formation and metastasis in different cancer types. The aim of this study is to explore the correlation of blood coagulation tests for various clinicopathologic factors in patients with metastatic pancreatic adenocarcinoma (MPA). MATERIAL: A total of 17 MPA patients were enrolled into the study. All the patients were treatment-naive. Pretreatment blood coagulation tests including prothrombin time, activated partial thromboplastin time (APTT), international normalized ratio (INR), D-dimer, fibrinogen levels, and platelet counts were evaluated. Control group comprised 50 age- and sex-matched individuals without history of malignancy and coagulation disorder. RESULTS: Median age of diagnosis was 59 years old (range, 35-72). The plasma level of all coagulation factors revealed statistically significant difference between patient and control group ($p < 0.01$). Anemic patients had associated with higher D-dimer levels ($p = 0.001$). Similarly, the ones with elevated serum CA19-9 exhibited significantly higher D-dimer values ($p = 0.011$). For APTT, significant differences were found in both between gender of patients ($p = 0.01$) and response to chemotherapy ($p = 0.01$). The patients with elevated erythrocyte sedimentation rates had associated with higher INR ($p = 0.05$). Univariate analysis of survival revealed that the patients with unresponsive to chemotherapy ($p = 0.06$) and higher INR ($p = 0.078$) had poor overall outcome. CONCLUSION: Serum D-dimer level is elevated among MPA patients with higher serum CA19-9 and higher INR levels seem to be a poor prognostic factor in MPA.

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[338]

TÍTULO / TITLE: - Early acute pancreatitis in a child with compound heterozygosis F508/R1438W/Y1032C cystic fibrosis: a case report.

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

REVISTA / JOURNAL: - J Med Case Rep. 2013 Jul 24;7(1):188. doi: 10.1186/1752-1947-7-188.

●● Enlace al texto completo (gratuito o de pago) 1186/1752-1947-7-188

AUTORES / AUTHORS: - Leonardi S; Pratico AD; Rotolo N; Di Dio G; Lionetti E; La Rosa M

INSTITUCIÓN / INSTITUTION: - Department of Medical and Pediatric Science, Unit of Broncho-Pneumology and Cystic Fibrosis, University of Catania, Via Santa Sofia 78, Catania 95123, Italy. leonardi@unict.it.

RESUMEN / SUMMARY: - INTRODUCTION: Recent studies suggest an important role of the cystic fibrosis transmembrane conductance regulator gene in the

development of pancreatitis. It occurs approximately in 20% of patients with cystic fibrosis and almost exclusively in pancreatic sufficient people. Newborn screening and improved panels of deoxyribonucleic acid mutation analysis techniques are revealing more rare and nonclassical pictures of the disease, generally associated with pancreatic sufficiency and with an increased risk of developing pancreatitis. Mutations R1438 and Y1032 are considered rare mutations, and, when singularly associated with F508, lead to a mild phenotype with pancreatic sufficiency and no detectable respiratory involvement. CASE PRESENTATION: We present the case of a Caucasian girl, aged six years, whose genotype was characterized by three different mutations F508, R1438W and Y1032C, never reported, together, in the same patient. She presented with a positive immunoreactive trypsinogen screening, a borderline sweat test, and, in the first years, a favorable pulmonary course, and pancreatic sufficiency. At the age of six years, she presented with a sudden episode of acute abdominal pain, anorexia and fever. A diagnosis of pancreatitis was made after clinical and laboratory examinations. Venous rehydration, bowel rest and therapy with ursodeoxycholic acid resulted in complete remission.The treatment was successful, with normalization of her symptoms and laboratory parameters within four weeks. CONCLUSION: There has been a vast expansion in the understanding of the wide range of phenotypes associated with cystic fibrosis transmembrane conductance regulator dysfunction since the discovery of the cystic fibrosis transmembrane conductance regulator gene. The genotype-phenotype correlation in pancreatitis is rare compared to other organ manifestations, since this is seen almost exclusively among pancreatic sufficient patients with cystic fibrosis. Our study supports that compound heterozygosis F508-R1438W/Y1032C is a 'cystic fibrosis-causing genotype' characterized by an immunoreactive trypsinogen positive screening, abnormal sweat chloride testing, and pancreatic sufficiency, with an increased risk of acute pancreatitis at an early age.

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[339]

TÍTULO / TITLE: - Anti-tumour efficacy of capecitabine in a genetically engineered mouse model of pancreatic cancer.

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

REVISTA / JOURNAL: - PLoS One. 2013 Jun 28;8(6):e67330. doi: 10.1371/journal.pone.0067330. Print 2013.

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

1371/journal.pone.0067330

AUTORES / AUTHORS: - Courtin A; Richards FM; Bapiro TE; Bramhall JL; Neesse A; Cook N; Krippendorff BF; Tuveson DA; Jodrell DI

INSTITUCIÓN / INSTITUTION: - Pharmacology and Drug Development Group, Cancer Research UK Cambridge Research Institute, Cambridge, United Kingdom ; University of Cambridge Department of Oncology, Cambridge, United Kingdom, Cambridge, United Kingdom.

RESUMEN / SUMMARY: - Capecitabine (CAP) is a 5-FU pro-drug approved for the treatment of several cancers and it is used in combination with gemcitabine (GEM) in the treatment of patients with pancreatic adenocarcinoma (PDAC). However, limited pre-clinical data of the effects of CAP in PDAC are available to support the use of the GEMCAP combination in clinic. Therefore, we investigated the pharmacokinetics and the efficacy of CAP as a single agent first and then in combination with GEM to assess the utility of the GEMCAP therapy in clinic. Using a model of spontaneous PDAC occurring in Kras(G12D); p53(R172H); Pdx1-Cre (KPC) mice and subcutaneous allografts of a KPC PDAC-derived cell line (K8484), we showed that CAP achieved tumour concentrations (approximately 25 microM) of 5-FU in both models, as a single agent, and induced survival similar to GEM in KPC mice, suggesting similar efficacy. In vitro studies performed in K8484 cells as well as in human pancreatic cell lines showed an additive effect of the GEMCAP combination however, it increased toxicity in vivo and no benefit of a tolerable GEMCAP combination was identified in the allograft model when compared to GEM alone. Our work provides pre-clinical evidence of 5-FU delivery to tumours and anti-tumour efficacy following oral CAP administration that was similar to effects of GEM. Nevertheless, the GEMCAP combination does not improve the therapeutic index compared to GEM alone. These data suggest that CAP could be considered as an alternative to GEM in future, rationally designed, combination treatment strategies for advanced pancreatic cancer.

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[340]

TÍTULO / TITLE: - Receptivity and preferences of pancreatic cancer family members for participating in lifestyle programs to reduce cancer risk.

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

REVISTA / JOURNAL: - Hered Cancer Clin Pract. 2013 May 31;11(1):3. doi: 10.1186/1897-4287-11-3.

●● Enlace al texto completo (gratuito o de pago) 1186/1897-4287-11-3

AUTORES / AUTHORS: - Howell LA; Sinicrope PS; Brockman TA; Patten CA; Decker PA; Ehlers SL; Nadeau A; Rabe KG; Breitkopf CR; Petersen GM

INSTITUCIÓN / INSTITUTION: - Department of Psychology and Psychiatry, Mayo Clinic Rochester, Rochester, MN, USA. patten.christi@mayo.edu.

RESUMEN / SUMMARY: - BACKGROUND: Cancer is a shared family experience that might provide an opportunity for lifestyle change among at-risk family members. The purpose of this study was to assess receptivity and preferences for cancer risk reduction programs among at-risk family members with two or more relatives affected with pancreas cancer. METHODS: We surveyed 401 at-risk family members in an existing pancreatic cancer family registry. Participants completed a mailed survey which examined demographic, medical, and psychosocial correlates of willingness to participate in lifestyle cancer risk reduction programs. Multivariable generalized estimating equation approaches were used to model preferences. RESULTS: Overall, 85% (n = 342) of at-risk

family members were receptive to lifestyle cancer risk reduction programs. Participant preferred programs focused on nutrition (36%, n = 116) and weight management (33%, n = 108), with Web/Internet (46%, n = 157) being the most preferred delivery channel. Most respondents preferred to participate in programs with their family or friends (74%, n = 182), rather than alone (25%, n = 85). In multivariable analysis, younger age (p = 0.008) and higher perceived likelihood of developing cancer (p = 0.03) were associated with willingness to participate in lifestyle programs. CONCLUSIONS: Family members of those with pancreatic cancer are receptive to cancer risk reduction programs focusing on nutrition and weight management delivered via the internet. Further research is indicated to determine how to best incorporate a family-based approach when designing lifestyle intervention programs.

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[341]

TÍTULO / TITLE: - Artemisinin as a chinese medicine, selectively induces apoptosis in pancreatic tumor cell line.

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

REVISTA / JOURNAL: - Chin J Integr Med. 2013 Jun 15.

●● Enlace al texto completo (gratuito o de pago) 1007/s11655-013-1454-2

AUTORES / AUTHORS: - Noori S; Hassan ZM; Farsam V

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, 1985717443, Iran, shnoori@sbmu.ac.ir.

RESUMEN / SUMMARY: - OBJECTIVE: To investigate the possible mechanism through which Artemisinin induced apoptosis in pancreatic cell line. METHODS: Column chromatography, thin layer chromatography (TLC) and proton NMR spectroscopy were used to purify Artemisinin. The flowcytometry was employed to detect apoptosis and reactive oxygen species (ROS). RESULTS: The results indicated that 50% inhibiting concentration (IC50 value) for pancreatic cell line (RIN) was 45 mumol/L of Artemisinin. Artemisinin had no cytotoxic effect on the growth of peripheral blood lymphocytes. The mechanism of apoptosis was evaluated by measuring intracellular ROS. It was shown that Artemisinin-induced apoptosis occurred independently of the binding of CD95L to CD95 receptor in the RIN cells. Moreover, Artemisinin, in a dose-dependent manner, could significantly increase the level of ROS. CONCLUSION: Artemisinin can induce apoptosis in the RIN cells via the generation of ROS and triggering the intrinsic pathway of cell death.

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[342]

TÍTULO / TITLE: - Pitfall in follow-up imaging of pancreatic neuroendocrine tumor by somatostatin receptor PET.

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

REVISTA / JOURNAL: - Neuro Endocrinol Lett. 2013;34(4):273-4.

AUTORES / AUTHORS: - Reindl O; Loidl A; Franz B; Hofer JF; Pichler R
INSTITUCIÓN / INSTITUTION: - Department of Surgery, Hospital Freistadt, Austria.
RESUMEN / SUMMARY: - 56-year old woman was operated of a pancreatic NET in May 2011. Abdominal pain had led to imaging and consecutively the finding of cholecystolithiasis and the tumor. The gall bladder, left hemi-pancreas, regional lymph nodes and the (unintentional injured) spleen were resected. At routine control examination in October 2012 CT presented three contract enhancing intra-abdominal lesions with a diameter of 2-3.5 cm. Consecutively 68Ga-DOTA-NOC PET-CT showed high tracer uptake (SUV 10-12) at these lesions. Therefore a relapse of the neuro-endocrine tumor was suspected. After reoperation in December 2012 histology did not reveal any sign of neuroendocrine tumor but identified spleen tissue most probably caused by splenosis accidentally seeded at the first operation. Physiologically the spleen is highly avid at 68Ga-DOTATOC PET, but splenosis presents with less standard uptake value. In our case the described lesions presented with an SUV quite comparable to that of neuroendocrine tumor tissue.

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[343]
TÍTULO / TITLE: - Changes in the immune cell population and cell proliferation in peripheral blood after gemcitabine-based chemotherapy for pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Transl Oncol. 2013 Jul 17.
●● Enlace al texto completo (gratuito o de pago) 1007/s12094-013-1079-0
AUTORES / AUTHORS: - Homma Y; Taniguchi K; Nakazawa M; Matsuyama R; Mori R; Takeda K; Ichikawa Y; Tanaka K; Endo I
INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery, Yokohama City University School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama, Kanagawa, 236-0004, Japan.
RESUMEN / SUMMARY: - PURPOSE: Regulatory T cells (Tregs) play a role in the immunosuppressive state in pancreatic cancer patients. We aimed to evaluate the changes of immune cells population including Tregs caused by gemcitabine (GEM)-based chemotherapy. METHODS: Fifty-three patients with pancreatic cancer were enrolled in this study, of which 32 received GEM- based chemotherapy. Blood samples were collected before and at least 2 weeks after the last dose of chemotherapy. The peripheral blood mononuclear cells (PBMCs) were subjected to flow cytometry analysis after labeling with anti-CD4, anti-CD25, and anti-Foxp3 antibodies. Other lymphocytes and NK cell markers were also measured. The proliferative capacity of PBMCs stimulated with anti-CD3 was analyzed using H3 thymidine. RESULTS: The percentage and number of Tregs were significantly decreased after chemotherapy ($p = 0.032$, $p = 0.003$, respectively). The other immune cells and the proliferative capacity did not change. CONCLUSION: This study showed that GEM-based chemotherapy produced an immunomodulatory effect via the depletion of Tregs.

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[344]

TÍTULO / TITLE: - ppENK Gene Methylation Status in the Development of Pancreatic Carcinoma.

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

REVISTA / JOURNAL: - Gastroenterol Res Pract. 2013;2013:130927. doi: 10.1155/2013/130927. Epub 2013 May 28.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/130927

AUTORES / AUTHORS: - Yang L; Yang H; Li J; Hao J; Qian J

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Beijing Chaoyang Hospital, Capital University of Medical Sciences, Beijing 100020, China.

RESUMEN / SUMMARY: - Objective. To explore the association of hypermethylation of the proenkephalin gene (ppENK) with pancreatic carcinoma and to identify the effects of a demethylating agent on pancreatic cell lines. Method. Human pancreatic cancer tissues and five pancreatic carcinoma cell lines, as well as normal pancreatic tissue, were used. ppENK methylation status was detected by MS-PCR (methylation-specific PCR). Results. Methylation of ppENK was detected in 90.3% (28/31) of the human pancreatic carcinoma tissues but was not seen in normal pancreatic tissue. There was no correlation between the extent of methylation of ppENK and the clinicopathological features of the pancreatic carcinomas. Methylated ppENK was detected in all the pancreatic cancer cell lines and was associated with loss of mRNA expression in the pancreatic carcinoma cell lines and normal pancreatic tissue. After treatment with 5-aza-dC, methylated ppENK was not detected and the inhibition of ppENK mRNA expression was reversed. Conclusions. Inhibition of ppENK expression by a change in its methylation status plays an important role in pancreatic carcinogenesis. ppENK methylation is thus an important molecular event that distinguishes pancreatic carcinoma tissue from normal pancreatic tissue. Effects on cell growth, apoptosis, and the cell cycle may contribute to changes of ppENK methylation status.

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[345]

TÍTULO / TITLE: - Reolysin is a novel reovirus-based agent that induces endoplasmic reticular stress-mediated apoptosis in pancreatic cancer.

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

REVISTA / JOURNAL: - Cell Death Dis. 2013 Jul 18;4:e728. doi: 10.1038/cddis.2013.259.

●● Enlace al texto completo (gratuito o de pago) 1038/cddis.2013.259

AUTORES / AUTHORS: - Carew JS; Espitia CM; Zhao W; Kelly KR; Coffey M; Freeman JW; Nawrocki ST

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Cancer Therapy and Research Center, Institute for Drug Development, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA.

RESUMEN / SUMMARY: - Activating mutation of KRas is a genetic alteration that occurs in the majority of pancreatic tumors and is therefore an ideal therapeutic target. The ability of reoviruses to preferentially replicate and induce cell death in transformed cells that express activated Ras prompted the development of a reovirus-based formulation for cancer therapy called Reolysin. We hypothesized that Reolysin exposure would trigger heavy production of viral products leading to endoplasmic reticular (ER) stress-mediated apoptosis. Here, we report that Reolysin treatment stimulated selective reovirus replication and decreased cell viability in KRas-transformed immortalized human pancreatic duct epithelial cells and pancreatic cancer cell lines. These effects were associated with increased expression of ER stress-related genes, ER swelling, cleavage of caspase-4, and splicing of XBP-1. Treatment with ER stress stimuli including tunicamycin, brefeldin A, and bortezomib (BZ) augmented the anticancer activity of Reolysin. Cotreatment with BZ and Reolysin induced the simultaneous accumulation of ubiquitinated and viral proteins, resulting in enhanced levels of ER stress and apoptosis in both in vitro and in vivo models of pancreatic cancer. Our collective results demonstrate that the abnormal protein accumulation induced by the combination of Reolysin and BZ promotes heightened ER stress and apoptosis in pancreatic cancer cells and provides the rationale for a phase I clinical trial further investigating the safety and efficacy of this novel strategy.

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[346]

TÍTULO / TITLE: - Unresectable Pancreatic Ductal Adenocarcinoma in the Remnant Pancreas Diagnosed during Every-6-Month Surveillance after Resection of Branch Duct Intraductal Papillary Mucinous Neoplasm: A Case Report.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):450-3. doi: 10.6092/1590-8577/1494.

AUTORES / AUTHORS: - Tamura K; Ohtsuka T; Ideno N; Aso T; Kono H; Nagayoshi Y; Shindo K; Ushijima Y; Ueda J; Takahata S; Ito T; Oda Y; Mizumoto K; Tanaka M

INSTITUCIÓN / INSTITUTION: - Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University. Fukuoka, Japan. masaotan@surg1.med.kyushu-u.ac.jp.

RESUMEN / SUMMARY: - CONTEXT: There are few studies regarding the surveillance period and interval of resected or observed branch duct intraductal papillary mucinous neoplasms (IPMNs) of the pancreas in terms of early detection of concomitant pancreatic ductal adenocarcinoma. Despite a strict surveillance protocol, some patients are diagnosed with metastatic distinct ductal adenocarcinoma after resection of IPMN. CASE REPORT: We herein report a patient with unresectable pancreatic ductal adenocarcinoma that developed in the remnant pancreas 18 months after resection of branch duct

IPMN. Although the patient was surveyed every 6 months after the operation and imaging studies at 6 and 12 months postoperatively demonstrated no evidence of recurrence, invasive ductal adenocarcinoma with liver metastasis appeared 18 months after the operation. The patient subsequently underwent chemotherapy; however, he died 9 months after the diagnosis of metachronous pancreatic ductal adenocarcinoma. CONCLUSIONS: In some patients with branch duct IPMNs, 6-month surveillance seems to be insufficient to detect resectable concomitant pancreatic ductal adenocarcinoma. Therefore, identification of high-risk patients who require surveillance at shorter intervals is urgently needed.

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[347]

TÍTULO / TITLE: - Locally advanced pancreatic cancer. Looking beyond traditional chemotherapy and radiation.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):337-9. doi: 10.6092/1590-8577/1677.

AUTORES / AUTHORS: - Savir G; Huber KE; Saif MW

INSTITUCIÓN / INSTITUTION: - Tufts Medical Center. Boston, MA, USA. khuber@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - About a third of all pancreatic cancer is found to be locally advanced at the time of diagnosis, where the tumor is inoperable but remains localized to the pancreas and regional lymphatics. Sadly, this remains a universally deadly disease with progression to distant disease being the predominant mode of failure and average survival under one year. Optimal treatment of these patients continues to be an area of controversy, with chemotherapy alone being the treatment preference in Europe, and chemotherapy followed by chemoradiation in selected patients, preferred in the USA. The aim of this paper is to summarize the key abstracts presented at the 2013 ASCO Annual Meeting that address evolving approaches to the management of locally advanced pancreatic cancer. The late breaking abstract (#LBA4003) provided additional European data showing non-superiority of chemoradiation compared to chemotherapy in locally advanced pancreatic cancer patients without distant progression following 4 months of chemotherapy. Another late breaking abstract, (#LBA4004), unfortunately showed a promising new complement to gemcitabine and capecitabine using immunotherapy in the form of a T-helper vaccine did not translate to improved survival in the phase III setting.

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[348]

- CASTELLANO -

TÍTULO / TITLE: Ruolo della TCMD e della RM nella valutazione preoperatoria dei tumori endocrini non funzionanti del pancreas.

TÍTULO / TITLE: - Preoperative assessment of nonfunctioning pancreatic endocrine tumours: role of MDCT and MRI.

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

REVISTA / JOURNAL: - Radiol Med. 2013 Jun 26.

●● Enlace al texto completo (gratuito o de pago) 1007/s11547-013-0956-5

AUTORES / AUTHORS: - Foti G; Boninsegna L; Falconi M; Mucelli RP

INSTITUCIÓN / INSTITUTION: - Dipartimento di Radiologia, Ospedale Sacrocuore Don Calabria, Via don A. Sempreboni 5, 37024, Negrar, Italy, gfoti81@yahoo.it.

RESUMEN / SUMMARY: - PURPOSE: This study was done to compare the diagnostic accuracy of multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI) in the preoperative assessment of nonfunctioning pancreatic endocrine tumours (NFPET). MATERIALS AND METHODS: Fifty-one patients (25 men, 26 women; mean age, 52 years), preoperatively investigated by both MDCT and MRI and subsequently operated on with a histological diagnosis of NFPET, were included in this study. MDCT and MRI accuracy in evaluating location, size, margins, baseline density/signal intensity, structure, pattern of enhancement, peak enhancement phase, involvement of main pancreatic duct, involvement of adjacent organs, infiltration of peritumoural vessels, involvement of locoregional lymph nodes, and liver metastases was compared using Pearson correlation, Mann-Whitney and chi-square tests. A value of $p<0.05$ was considered statistically significant. RESULTS: MDCT and MRI had similar accuracy in assessing size, margins, baseline density/signal intensity, structure, pattern of enhancement, peak enhancement phase, involvement of main pancreatic duct, involvement of adjacent organs, involvement of locoregional lymph nodes, and liver metastases ($p>0.05$). MDCT was superior to MRI in evaluating the infiltration of peritumoural vessels ($p=0.025$). CONCLUSIONS: MDCT performed better than MRI in assessing vascular involvement and should be considered the best imaging tool for preoperative evaluation of NFPET.

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[349]

TÍTULO / TITLE: - A case of pancreatic cancer in the setting of autoimmune pancreatitis with nondiagnostic serum markers.

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

REVISTA / JOURNAL: - Case Rep Surg. 2013;2013:809023. doi: 10.1155/2013/809023. Epub 2013 May 28.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/809023

AUTORES / AUTHORS: - Chandrasegaram MD; Chiam SC; Nguyen NQ; Ruszkiewicz A; Chung A; Neo EL; Chen JW; Worthley CS; Brooke-Smith ME

INSTITUCIÓN / INSTITUTION: - Hepatobiliary Unit, Royal Adelaide Hospital, North Terrace, Adelaide, SA 5000, Australia.

RESUMEN / SUMMARY: - Background. Autoimmune pancreatitis (AIP) often mimics pancreatic cancer. The diagnosis of both conditions is difficult

preoperatively let alone when they coexist. Several reports have been published describing pancreatic cancer in the setting of AIP. Case Report. The case of a 53-year-old man who presented with abdominal pain, jaundice, and radiological features of autoimmune pancreatitis, with a “sausage-shaped” pancreas and bulky pancreatic head with portal vein impingement, is presented. He had a normal serum IgG4 and only mildly elevated Ca-19.9. Initial endoscopic ultrasound-(EUS-) guided fine-needle aspiration (FNA) of the pancreas revealed an inflammatory sclerosing process only. A repeat EUS guided biopsy following biliary decompression demonstrated both malignancy and features of autoimmune pancreatitis. At laparotomy, a uniformly hard, bulky pancreas was found with no sonographically definable mass. A total pancreatectomy with portal vein resection and reconstruction was performed. Histology revealed adenosquamous carcinoma of the pancreatic head and autoimmune pancreatitis and squamous metaplasia in the remaining pancreas. Conclusion. This case highlights the diagnostic and management difficulties in a patient with pancreatic cancer in the setting of serum IgG4-negative, Type 2 AIP.

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[350]

TÍTULO / TITLE: - A case of spontaneous ruptured solid pseudopapillary tumor of pancreas resected by laparoscopic surgery.

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

REVISTA / JOURNAL: - Case Rep Med. 2013;2013:953240. doi: 10.1155/2013/953240. Epub 2013 Apr 30.

●● Enlace al texto completo (gratuito o de pago) 1155/2013/953240

AUTORES / AUTHORS: - Takamatsu S; Nagano H; Ohtsukasa S; Kawachi Y; Maruyama H

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Musashino Red Cross Hospital, 1-26-1 Kyounan-cho, Musashino-shi, Tokyo 180-8610, Japan.

RESUMEN / SUMMARY: - Solid pseudopapillary tumor (SPT) is an uncommon neoplasm of the pancreas. A rare case of spontaneous rupture of SPT is reported. A 13-year-old female felt acute abdominal pain without blunt abdominal trauma. Enhanced computed tomography (CT) revealed a tumor in the pancreas tail with fluid collection around it. The tumor was diagnosed as SPT with hemoperitoneum associated with spontaneous rupture. The bleeding was stopped conservatively and she was referred for surgery at three months after the rupture. At that time, CT revealed a tumor 4 cm in diameter, which protruded from pancreas tail without distant metastases. Since peritoneal dissemination was not seen on intraoperative exploration, laparoscopic enucleation was performed. Pathologically, the tumor was diagnosed as SPT with rupture of the capsule of tumor, and complete resection was confirmed. The patient has been followed up for two years, and she is alive without recurrence.

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[351]

TÍTULO / TITLE: - Laparoscopic minor pancreatic resections (enucleations/atypical resections). A long-term appraisal of a supposed mini-invasive approach.

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

REVISTA / JOURNAL: - Wideochir Inne Tech Malo Inwazyjne. 2013 Jun;8(2):117-29. doi: 10.5114/wiitm.2011.32863. Epub 2013 Jan 21.

●● Enlace al texto completo (gratuito o de pago) 5114/wiitm.2011.32863

AUTORES / AUTHORS: - Costi R; Randone B; Mal F; Basato S; Levard H; Gayet B

INSTITUCIÓN / INSTITUTION: - Departement de Pathologie Digestive, Institut Mutualiste Montsouris, Paris, France ; Dipartimento di Scienze Chirurgiche, Universita degli Studi di Parma, Parma, Italia.

RESUMEN / SUMMARY: - INTRODUCTION: A few retrospective, small, often multicentric studies show encouraging results of laparoscopic minor pancreatic surgery, but do not allow for an evaluation of feasibility and effectiveness. AIM: Evaluation of the results of laparoscopic minor pancreatic resections (LMPR), including atypical resections and enucleations. MATERIAL AND METHODS: The outcome of all consecutive patients undergoing LMPR in a tertiary care university hospital specializing in the laparoscopic approach to solid organs (I.M.M., Paris - France) was retrospectively evaluated by the analysis of operating time, blood loss, conversion, morbidity, stay and late outcome. RESULTS: Thirty-three patients underwent LMPR (29 enucleations and 4 atypical resections) for various diseases. The conversion rate was 21%, mean operating time 189 min, and mean blood loss 133 ml. Morbidity was 60%; 10 patients (30%) presented a pancreatic fistula. Pancreatic fistula was independent of type of resection, technique of pancreas section, management of enucleated surface and somatostatin administration. Median stay for enucleations was 18 days. Mean follow-up was 61 months. CONCLUSIONS: Laparoscopic pancreatic enucleation is feasible and safe, with no mortality, no lengthening of operating time and a high success rate. Conversely, it does not imply a reduction in complications or hospital stay at the present state of the art.

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[352]

TÍTULO / TITLE: - The myeloid response to pancreatic carcinogenesis is regulated by the receptor for advanced glycation end-products.

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

REVISTA / JOURNAL: - Oncoimmunology. 2013 May 1;2(5):e24184.

●● Enlace al texto completo (gratuito o de pago) 4161/onci.24184

AUTORES / AUTHORS: - Vernon PJ; Zeh Iii HJ; Lotze MT

INSTITUCIÓN / INSTITUTION: - Department of Surgery; Hillman Cancer Center; University of Pittsburgh Cancer Institute; Pittsburgh, PA USA.

RESUMEN / SUMMARY: - We identified a critical role for receptor for advanced glycation end products (RAGE) in the intratumoral accumulation of myeloid-derived suppressor cells (MDSCs) during pancreatic carcinogenesis. The

absence of RAGE markedly delayed neoplasia and limited MDSC accumulation in mice expressing an oncogenic variant of Kras. In spite of MDSCs, these mice accumulated non-immunosuppressive macrophages. Thus, RAGE regulates carcinogenesis and consequent myeloid responses.

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[353]

TÍTULO / TITLE: - Powerful Inhibition of Experimental Human Pancreatic Cancers by Receptor Targeted Cytotoxic LH-RH analog AEZS-108.

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

REVISTA / JOURNAL: - Oncotarget. 2013 May;4(5):751-60.

AUTORES / AUTHORS: - Szepeshazi K; Schally AV; Block NL; Halmos G; Nadji M; Szalontay L; Vidaurre I; Abi-Chaker A; Rick FG

INSTITUCIÓN / INSTITUTION: - Veterans Affairs Medical Center, Miami, FL.

RESUMEN / SUMMARY: - Pancreatic carcinoma is one of the cancers with the worse prognosis, thus any therapeutic improvement is imperative. Cytotoxic LH-RH analog, AN-152 (proprietary designation, AEZS-108), consisting of doxorubicin (DOX) conjugated to D-Lys6LH-RH, is now in clinical trials for targeted therapy of several sex hormone-dependent tumors that express LH-RH receptors. We investigated LH-RH receptors in human pancreatic carcinoma and the effects of AN-152 (AEZS-108) on experimental pancreatic cancers. We determined LH-RH receptor presence in human pancreatic cancer samples by immunohistochemistry and, in three human pancreatic cancer lines (SW-1990, Panc-1 and CFPAC-1), by binding assays and Western blotting. The effects of the cytotoxic LH-RH analog were investigated on growth of these same cancer lines xenografted into nude mice. We also analyzed differences between the antitumor effects of the cytotoxic analog and its cytotoxic radical alone, doxorubicin (DOX), on the expression of cancer-related genes by PCR arrays. LH-RH receptors were expressed in two randomly selected surgically removed human pancreatic cancer samples and in all three cancer lines. Cytotoxic LH-RH analogs powerfully inhibited growth of all three tumor lines in nude mice; AN-152 was significantly stronger than DOX on Panc-1 and CFPAC-1 cancers. PCR array showed that cytotoxic LH-RH analog AN-152 affected the expression of genes associated with cellular migration, invasion, metastasis and angiogenesis more favorably than DOX, however the changes in gene expression varied considerably among the three cancer lines. Cytotoxic LH-RH analog, AEZS-108, may be a useful agent for the treatment of LH-RH receptor positive advanced pancreatic carcinoma.

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[354]

TÍTULO / TITLE: - Multiple Glucagon-Producing Pancreatic Neuroendocrine Tumors in a Horse (Equus caballus).

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

REVISTA / JOURNAL: - Vet Pathol. 2013 Jun 17.

●● Enlace al texto completo (gratuito o de pago)
1177/0300985813492803

AUTORES / AUTHORS: - Herbach N; Nagel L; Zwick T; Hermanns W

INSTITUCIÓN / INSTITUTION: - Center for Clinical Veterinary Medicine, Ludwig-Maximilians-University, Munich, Germany.

RESUMEN / SUMMARY: - Pancreatic neuroendocrine tumors of glucagon-producing cells are extremely rare in domestic animals. In this report, we describe for the first time, to our knowledge, the incidental finding of multiple glucagon-producing neuroendocrine tumors of the pancreas of a horse. The animal was euthanized due to severe local infection after tooth extraction. On postmortem examination, multiple white nodules of up to 4 cm in diameter were observed in the pancreas. Histologically, pancreatic nodules had the appearance of neuroendocrine neoplasms with positive immunoreactivity for glucagon, synaptophysin, chromogranin A, and neuron-specific enolase. Electron microscopy revealed numerous electron-dense granules, similar to those observed in normal pancreatic alpha cells, in the neoplastic cells. In addition, the left adrenal gland showed multiple hyperplastic foci and adenomas in the medulla that were identified as pheochromocytomas. Based on the morphologic appearance and immunohistochemical staining pattern of pancreatic nodules, a diagnosis of multiple glucagon-producing neuroendocrine tumors was made.

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[355]

- CASTELLANO -

TÍTULO / TITLE: Tumori intraduttali papillari mucino-secernenti (IPMN) dei dotti pancreatici secondari: aspetti RM ed evoluzione nel tempo.

TÍTULO / TITLE: - Multifocal branch-duct intraductal papillary mucinous neoplasms (IPMNs) of the pancreas: magnetic resonance (MR) imaging pattern and evolution over time.

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

REVISTA / JOURNAL: - Radiol Med. 2013 Jun 26.

●● Enlace al texto completo (gratuito o de pago) 1007/s11547-013-0945-8

AUTORES / AUTHORS: - Castelli F; Bosetti D; Negrelli R; Di Paola V; Zantedeschi L; Ventriglia A; Manfredi R; Mucelli RP

INSTITUCIÓN / INSTITUTION: - Istituto di Radiologia, Azienda Ospedaliero Universitaria Integrata - Policlinico “G.B. Rossi”, P.le L.A. Scuro 10, 37134, Verona, Italy.

RESUMEN / SUMMARY: - PURPOSE: The aim of our study was to follow the evolution over time of multifocal intraductal papillary mucinous neoplasms (IPMN) of the pancreatic duct side branches by means of magnetic resonance imaging (MRI). MATERIALS AND METHODS: A total of 155 patients with

multifocal IPMN of the side branches were examined with MRI and MR cholangiopancreatography (MRI/MRCP). Inclusion criteria were patients with >/=2 dilated side branches involving any site of the parenchyma; presence of communication with the main pancreatic duct and previous investigations by MRI/MRCP within at least six months. Median follow-up was 25.8 months (range, 12-217). Patients with a follow-up period shorter than 12 months (n=33) and those with a diagnosis of multifocal IPMN of the side branches without any follow-up (n=14) were excluded from the study. The final study population thus comprised 108 patients. A double, quantitative and qualitative, analysis was carried out. The quantitative image analysis included: number of dilated side branches in the head-uncinate process and body-tail; maximum diameter of lesions in the head-uncinate process; maximum diameter in the body-tail; maximum diameter of the main pancreatic duct in the head and body-tail. The qualitative image analysis included: presence of malformations or anatomical variants of the pancreatic ductal system; site of the lesions (head-uncinate process, body-tail, ubiquitous, bridge morphology); presence of gravity-dependent intraluminal filling defects; presence of enhancing mural nodules. RESULTS: At diagnosis, the mean number of cystic lesions of the side branches was 7.09. The mean diameter of the cystic lesions was 13.7 mm. The mean diameter of the main pancreatic duct was 3.6 mm. At follow-up, the mean number of cystic lesions was 7.76. The mean diameter of the cystic lesions was 13.9 mm. The mean diameter of the main pancreatic duct was 3.7 mm. Intraluminal filling defects in the side branches were seen in 18/108 patients (16.6%); enhancing mural nodules were seen in 3/108 patients (2.7%). CONCLUSIONS: Multifocal IPMN of the branch ducts shows a very slow growth and evolution over time. In our study, only 3/108 patients showed mural nodules which, however, did not require any surgical procedure, indicating that careful nonoperative management may be safe and effective in asymptomatic patients.

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[356]

TÍTULO / TITLE: - Aberrant right hepatic artery in pancreaticoduodenectomy for adenocarcinoma: impact on resectability and postoperative outcomes.

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

REVISTA / JOURNAL: - HPB (Oxford). 2013 Jun 19. doi: 10.1111/hpb.12120.

●● Enlace al texto completo (gratuito o de pago) 1111/hpb.12120

AUTORES / AUTHORS: - Kim PT; Temple S; Atenafu EG; Cleary SP; Moulton CA; McGilvray ID; Gallinger S; Greig PD; Wei AC

INSTITUCIÓN / INSTITUTION: - Department of Surgical Oncology, University Health Network, Toronto, ON, Canada; Department of Surgery, University of Toronto, Toronto, ON, Canada.

RESUMEN / SUMMARY: - OBJECTIVES: An aberrant right hepatic artery (aRHA) may pose technical and oncologic challenges during pancreaticoduodenectomy (PD) for pancreatic adenocarcinoma (PA) as a result of its proximity to the head of the pancreas. The aim of this study was to assess the impact of an aRHA on

resectability, and perioperative and oncologic outcomes after PD for PA. METHODS: An 11-year retrospective cohort study was conducted. A total of 289 patients with PA scheduled for PD with intent for resection were included in the study. RESULTS: Of 289 patients, 249 underwent PD and 40 were found to have unresectable tumours. Incidences of aRHA in the resectable (14.9%) and unresectable (7.5%) groups were similar (P = 0.2); the main reasons for aborting PD were not directly related to the presence of an aRHA. In patients who underwent resection, complications occurred more frequently in the standard PD group (41.5% versus 24.3%; P = 0.04), but there was no difference in rates of positive margin (R1) resection (10.8% versus 16.0%; P = 0.4) or median overall survival (17 months versus 23 months; P = 0.1) between patients with and without an aRHA. CONCLUSIONS: The presence of an aRHA in patients with PA does not affect resectability. In patients with resectable tumours, the presence of an aRHA does not increase morbidity or R1 resection rates and does not impact on overall survival.

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[357]

TÍTULO / TITLE: - Proposal for a standardized pathology report of gastroenteropancreatic neuroendocrine tumors: prognostic significance of pathological parameters.

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

REVISTA / JOURNAL: - Korean J Pathol. 2013 Jun;47(3):227-37. doi: 10.4132/KoreanJPathol.2013.47.3.227. Epub 2013 Jun 25.

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

4132/KoreanJPathol.2013.47.3.227

AUTORES / AUTHORS: - Cho MY; Sohn JH; Jin SY; Kim H; Jung ES; Kim MJ; Kim KM; Kim WH; Kim JM; Kang YK; Choi JH; Kang DY; Kim YW; Choi EH

RESUMEN / SUMMARY: - BACKGROUND: There is confusion in the diagnosis and biological behaviors of gastroenteropancreatic neuroendocrine tumors (GEP-NETs), because of independently proposed nomenclatures and classifications. A standardized form of pathology report is required for the proper management of patients. METHODS: We discussed the proper pathological evaluation of GEP-NET at the consensus conference of the subcommittee meeting for the Gastrointestinal Pathology Study Group of the Korean Society of Pathologists. We then verified the prognostic significance of pathological parameters from our previous nationwide collection of pathological data from 28 hospitals in Korea to determine the essential data set for a pathology report. RESULTS: Histological classification, grading (mitosis and/or Ki-67 labeling index), T staging (extent, size), lymph node metastasis, and lymphovascular and perineural invasion were significant prognostic factors and essential for the pathology report of GEP-NET, while immunostaining such as synaptophysin and chromogranin may be optional. Furthermore, the staging system, either that of the 2010 American Joint Cancer Committee (AJCC) or the European Neuroendocrine Tumor Society (ENETS), should be specified,

especially for pancreatic neuroendocrine neoplasms. CONCLUSIONS: A standardized pathology report is crucial for the proper management and prediction of prognosis of patients with GEP-NET.

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[358]

TÍTULO / TITLE: - Alternative arterial reconstruction after extended pancreatectomy. Case report and some considerations of locally advanced pancreatic cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):432-7. doi: 10.6092/1590-8577/1468.

AUTORES / AUTHORS: - Ielpo B; Ferri V; Caruso R; Duran H; Diaz E; Fabra I; Oliva C; Olivares S; Quijano Y; Vicente E

INSTITUCIÓN / INSTITUTION: - General Surgery Department, Madrid Sanchinarro University Hospital, San Pablo University. Madrid, España. ielpo.b@gmail.com.

RESUMEN / SUMMARY: - CONTEXT: The clinical benefits of distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic body cancer remains controversial and, therefore, declared unresectable in most cases. Appleby first described extended distal pancreatectomy with celiac axis resection for locally advanced gastric cancer. CASE REPORT: We report a case of a 65-year-old female who presented a locally advanced pancreatic carcinoma with infiltration of celiac axis. After radio-chemo neoadjuvant treatment, the patient underwent exploratory laparoscopy and subsequent distal pancreatectomy with en bloc resection of celiac axis. Arterial reconstruction was necessary as hepatic flow was not adequate, determined by intraoperative Doppler ultrasonography. It consisted of end to end anastomosis with prosthetic graft between hepatic artery directly to the aorta, as an atheromatous plaque was at the origin of the celiac axis. The postoperative course was uneventful with a perfect relief of pain. She presents a long term survival of 36 months, very exceptional for this type of disease. CONCLUSION: The particularity of this case is not only the surgical treatment, rarely offered to these patients, but also and especially the subsequent vascular reconstruction. To our knowledge, this is the first report of this type of arterial reconstruction. Besides, we briefly discuss the recent advances in results of extended distal pancreatectomy with arterial resection for locally advanced pancreatic carcinoma.

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[359]

TÍTULO / TITLE: - Antagonistic Effects of Anti-EMMPRIN Antibody When Combined with Chemotherapy Against Hypovascular Pancreatic Cancers.

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

REVISTA / JOURNAL: - Mol Imaging Biol. 2013 Jul 9.

●● Enlace al texto completo (gratuito o de pago) 1007/s11307-013-0665-4

AUTORES / AUTHORS: - Kim H; Rigell CJ; Zhai G; Lee SK; Samuel SL; Martin A; Umphrey HR; Stockard CR; Beasley TM; Buchsbaum DJ; Li LS; Boothman DA; Zinn KR

INSTITUCIÓN / INSTITUTION: - Department of Radiology, University of Alabama at Birmingham, Birmingham, AL, 35294-0019, USA, Hyunki@uab.edu.

RESUMEN / SUMMARY: - PURPOSE: To examine the antagonistic effects of anti-extracellular matrix metalloprotease inducer (anti-EMMPRIN) antibody when combined with chemotherapy using a hypovascular pancreatic tumor model. PROCEDURES: Severely compromised immunodeficient mice bearing orthotopic MIA PaCa-2 tumors were used (five to six animals per group). Dynamic contrast-enhanced magnetic resonance imaging was used to examine the relationship between tumor vascularity and size. Therapy was initiated when tumors were hypovascular. Treatments included: (1) gemcitabine alone, (2) anti-EMMPRIN antibody alone, and (3) combination, each for 2 weeks. Additionally, another treatment arm included beta-lapachone, an NAD(P)H/quinone 1 (NQO1) bioactivated agent. 18F-fluoro-D-glucose-positron emission tomography/computed tomography imaging was used weekly to monitor therapeutic effects. RESULTS: Gemcitabine or anti-EMMPRIN monotherapy significantly delayed tumor growth, but the combination therapy showed an antagonistic effect. Similarly, tumor growth was significantly suppressed by beta-lapachone alone, and additive effects were noted when combined with gemcitabine, but the therapeutic efficacy was reduced when anti-EMMPRIN antibody was added. CONCLUSIONS: Anti-EMMPRIN antibody with chemotherapy in hypovascular tumors results in antagonistic effects.

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[360]

TÍTULO / TITLE: - Three cases of concomitant intraductal papillary mucinous neoplasm and pancreatic neuroendocrine tumour.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):423-7. doi: 10.6092/1590-8577/1491.

AUTORES / AUTHORS: - Tewari N; Zaitoun AM; Lindsay D; Abbas A; Ilyas M; Lobo DN

INSTITUCIÓN / INSTITUTION: - Division of Gastrointestinal Surgery, Nottingham Digestive Diseases Centre National Institute for Health Research Biomedical Research Unit, University of Nottingham, Queen's Medical Centre. Nottingham, United Kingdom. dileep.lobo@nottingham.ac.uk.

RESUMEN / SUMMARY: - CONTEXT: Intraductal papillary mucinous neoplasms (IPMNs) are uncommon tumours which can be associated with pancreatic and extrapancreatic malignancies. The association of IPMN and neuroendocrine tumours of the pancreas has been reported previously but is exceedingly rare. CASE REPORT: We report three cases of IPMN treated with total pancreatectomy/extended distal pancreatectomy. Histopathological analysis of the resected specimens revealed concomitant IPMN and neuroendocrine

tumour. Two patients had adenocarcinoma as well. CONCLUSIONS: The presence of an IPMN may place the entire pancreas at risk of developing other tumour types and vigilance during all stages of management is necessary to ensure optimal treatment.

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[361]

TÍTULO / TITLE: - A Rare Case of Primary Pancreatic Hodgkin Lymphoma.

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

REVISTA / JOURNAL: - J Gastrointest Cancer. 2013 Jul 3.

●● Enlace al texto completo (gratuito o de pago) 1007/s12029-013-9521-7

AUTORES / AUTHORS: - Parikh JG; Bilal M; Tombazzi C; Jackson BK; Dong H

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Veterans Affairs Medical Center, University of Tennessee Health Science Center, Memphis, TN, USA.

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[362]

TÍTULO / TITLE: - Pancreatic metastasis from mixed adenoneuroendocrine carcinoma of the uterine cervix: a case report.

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

REVISTA / JOURNAL: - Case Rep Oncol. 2013 May 9;6(2):256-62. doi: 10.1159/000351308. Print 2013 May.

●● Enlace al texto completo (gratuito o de pago) 1159/000351308

AUTORES / AUTHORS: - Nishimura C; Naoe H; Hashigo S; Tsutsumi H; Ishii S; Konoe T; Watanabe T; Shono T; Sakurai K; Takaishi K; Ikuta Y; Chikamoto A; Tanaka M; Iyama K; Baba H; Katabuchi H; Sasaki Y

INSTITUCIÓN / INSTITUTION: - Departments of Gastroenterology and Hepatology, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan.

RESUMEN / SUMMARY: - Metastatic cancers of the pancreas are rare, accounting for approximately 2-4% of all pancreatic malignancies. Renal cell carcinoma is the most common solid tumor that metastasizes to the pancreas. Here, we present a case of uterine cervical carcinoma metastasizing to the pancreas and review the literature regarding this rare event. A 44-year-old woman with a uterine cervical tumor had undergone radical hysterectomy and had been diagnosed pathologically with stage Ib mixed adenoneuroendocrine carcinoma in 2004. She underwent concurrent radiotherapy and chemotherapy postoperatively. Pulmonary metastases subsequently appeared in 2008 and 2011, and she underwent complete resection of the lung tumors by video-assisted thoracic surgery. Although she was followed up without any treatment and with no other recurrences, positron emission tomography revealed an area of abnormal uptake within the pancreatic body in 2012. Enhanced computed tomography demonstrated a 20-mm lesion in the pancreatic body and upstream pancreatic duct dilatation. Endoscopic ultrasonography-guided fine needle aspiration was performed and pathological examination suggested neuroendocrine carcinoma (NEC). On the basis of these results and the

patient's oncological background, lesions in the pancreatic body were diagnosed as secondary metastasis from the cervical carcinoma that had been treated 8 years earlier. No other distant metastases were visualized, and the patient subsequently underwent middle pancreatectomy. Pathological examination showed NEC consistent with pancreatic metastasis from the uterine cervical carcinoma. The patient has survived 7 months since the middle pancreatectomy without any signs of local recurrence or other metastatic lesions.

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[363]

TÍTULO / TITLE: - A case of intraductal papillary mucinous carcinoma found with acute obstructive suppurative pancreatic ductitis and liver abscess, and associated with a pancreatobiliary fistula.

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

REVISTA / JOURNAL: - Nihon Shokakibyo Gakkai Zasshi. 2013 Jul;110(7):1304-12.

AUTORES / AUTHORS: - Nishie H; Okumura F; Fukusada S; Inoue T; Kachi K; Anbe K; Natsume M; Nishi Y; Yoshimura N; Mizushima T; Sano H; Kajikawa M; Harada A; Naitoh I; Hayashi K; Nakazawa T

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Gifu Prefectural Tajimi Hospital.

RESUMEN / SUMMARY: - We report a rare case of intraductal papillary mucinous carcinoma (IPMC) with acute obstructive suppurative pancreatic ductitis (AOSPD), liver abscess, and pancreatobiliary fistula formation. A man in his sixties was admitted to our hospital with a chief complain of high grade fever and anorexia. CT and MRI revealed a multilocular cystic lesion in the pancreatic head, fistula formation between the common bile duct and this cystic lesion, and multiple liver abscess. We performed endoscopic nasopancreatic drainage for the AOSPD, endoscopic biliary drainage for the biliary flow obstruction, and percutaneous transhepatic drainage for the liver abscess. Klebsiella pneumoniae was detected in the culture of pancreatic juice and liver abscess, but not in the bile and blood culture. These culture studies revealed that the liver abscess was caused by AOSPD. The patient underwent pancreaticoduodenectomy for the IPMC. The pathological diagnosis was IPMC.

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[364]

TÍTULO / TITLE: - A case of metastatic gastric cancer secondary to pancreatic neuroendocrine tumor fifteen years after distal pancreatectomy.

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

REVISTA / JOURNAL: - Nihon Shokakibyo Gakkai Zasshi. 2013 Jul;110(7):1281-7.

AUTORES / AUTHORS: - Kinoshita O; Okamoto K; Konishi H; Komatsu S; Yasukawa S; Shiozaki A; Kubota T; Yasuda H; Konishi H; Kishimoto M; Konishi E; Yanagisawa A; Otsuji E

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Division of Digestive Surgery, Kyoto Prefectural University of Medicine.

RESUMEN / SUMMARY: - A 56-year-old man underwent distal pancreatectomy in July 1997, and chemotherapy was administered as adjuvant therapy. The histopathological diagnosis was a neuroendocrine tumor of the pancreas, NET G2 (Ki-67 labeling index: 3%), T2N0M0 stage IB, according to the TNM classification. In July 2011, follow-up endoscopic examination showed a submucosal tumor covered with almost normal gastric mucosa in the posterior wall of the upper stomach. Endoscopic ultrasound showed a heterogeneous-echoic submucosal tumor present at both the submucosal layer and the proper muscle layer. Abdominal enhanced CT revealed a 3-cm-diameter enhanced mass in the posterior wall of the upper stomach. We performed local resection of the gastric posterior wall. The histopathological diagnosis was a metastatic gastric tumor secondary to a pancreatic endocrine tumor, NET G2 (Ki-67 labeling index: 10%). In this paper, we report a rare case of metastatic gastric cancer secondary to a pancreatic neuroendocrine tumor 15 years after the first operation, together with a review of the literature.

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[365]

TÍTULO / TITLE: - Sonoporation-Enhanced Chemotherapy Significantly Reduces Primary Tumour Burden in an Orthotopic Pancreatic Cancer Xenograft.

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

REVISTA / JOURNAL: - Mol Imaging Biol. 2013 Jul 23.

●● Enlace al texto completo (gratuito o de pago) 1007/s11307-013-0672-5

AUTORES / AUTHORS: - Kotopoulis S; Delalande A; Popa M; Mamaeva V; Dimcevski G; Gilja OH; Postema M; Gjertsen BT; McCormack E

INSTITUCIÓN / INSTITUTION: - National Centre for Ultrasound in Gastroenterology, Haukeland University Hospital, Jonas Liesvei 65, 5021, Bergen, Norway.

RESUMEN / SUMMARY: - PURPOSE: Adenocarcinoma of the pancreas remains one of the most lethal human cancers. The high mortality rates associated with this form of cancer are subsequent to late-stage clinical presentation and diagnosis, when surgery is rarely possible and of modest chemotherapeutic impact. Survival rates following diagnosis with advanced pancreatic cancer are very low; typical mortality rates of 50 % are expected within 3 months of diagnosis. However, adjuvant chemotherapy improves the prognosis of patients even after palliative surgery, and successful newer neoadjuvant chemotherapeutical modalities have recently been reported. For patients whose tumours appear unresectable, chemotherapy remains the only option. During the past two decades, the nucleoside analogue gemcitabine has become the first-line chemotherapy for pancreatic adenocarcinoma. In this study, we aim to increase the delivery of gemcitabine to pancreatic tumours by exploring the effect of sonoporation for localised drug delivery of gemcitabine in

an orthotopic xenograft mouse model of pancreatic cancer. EXPERIMENTAL DESIGN: An orthotopic xenograft mouse model of luciferase expressing MIA PaCa-2 cells was developed, exhibiting disease development similar to human pancreatic adenocarcinoma. Subsequently, two groups of mice were treated with gemcitabine alone and gemcitabine combined with sonoporation; saline-treated mice were used as a control group. A custom-made focused ultrasound transducer using clinically safe acoustic conditions in combination with SonoVue® ultrasound contrast agent was used to induce sonoporation in the localised region of the primary tumour only. Whole-body disease development was measured using bioluminescence imaging, and primary tumour development was measured using 3D ultrasound. RESULTS: Following just two treatments combining sonoporation and gemcitabine, primary tumour volumes were significantly lower than control groups. Additional therapy dramatically inhibited primary tumour growth throughout the course of the disease, with median survival increases of up to 10 % demonstrated in comparison to the control groups. CONCLUSION: Combined sonoporation and gemcitabine therapy significantly impedes primary tumour development in an orthotopic xenograft model of human pancreatic cancer, suggesting additional clinical benefits for patients treated with gemcitabine in combination with sonoporation.

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[366]

TÍTULO / TITLE: - Performance of endoscopic ultrasound-guided fine needle aspiration in diagnosing pancreatic neuroendocrine tumors.

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

REVISTA / JOURNAL: - Cytojournal. 2013 May 29;10:10. doi: 10.4103/1742-6413.112648. Print 2013.

●● Enlace al texto completo (gratuito o de pago) 4103/1742-6413.112648

AUTORES / AUTHORS: - Bernstein J; Ustun B; Alomari A; Bao F; Aslanian HR; Siddiqui U; Chhieng D; Cai G

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Internal Medicine, Yale University, School of Medicine, New Haven, Connecticut, USA.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic neuroendocrine tumors (PNETs) are rare tumors of the pancreas, which are increasingly diagnosed by endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). In this retrospective study, we assessed the performance of EUS-FNA in diagnosing PNETs. MATERIALS AND METHODS: We identified 48 cases of surgically resected PNETs in which pre-operative EUS-FNA was performed. The clinical features, cytological diagnoses, and surgical follow-up were retrospectively reviewed. The diagnostic performance of EUS-FNA was analyzed as compared to the diagnosis in the follow-up. The cases with discrepancies between cytological diagnosis and surgical follow-up were analyzed and diagnostic pitfalls in discrepant cases were discussed. RESULTS: The patients were 20 male and 28 female with ages ranging from 15 years to 81 years (mean 57

years). The tumors were solid and cystic in 41 and 7 cases, respectively, with sizes ranging from 0.5 cm to 11 cm (mean 2.7 cm). Based on cytomorphologic features and adjunct immunocytochemistry results, when performed, 38 patients (79%) were diagnosed with PNET, while a diagnosis of suspicious for PNET or a diagnosis of neoplasm with differential diagnosis including PNET was rendered in the 3 patients (6%). One case was diagnosed as mucinous cystic neoplasm (2%). The remaining 6 patients (13%) had non-diagnostic, negative or atypical diagnosis. CONCLUSIONS: Our data demonstrated that EUS-FNA has a relatively high sensitivity for diagnosing PNETs. Lack of additional materials for immunocytochemical studies could lead to a less definite diagnosis. Non-diagnostic or false negative FNA diagnosis can be seen in a limited number of cases, especially in those small sized tumors.

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[367]

TÍTULO / TITLE: - Diagnostic error assessment and associated harm of endoscopic ultrasound-guided fine-needle aspiration of neuroendocrine neoplasms of the pancreas.

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

REVISTA / JOURNAL: - Cancer Cytopathol. 2013 Jul 9. doi: 10.1002/cncy.21332.

●● Enlace al texto completo (gratuito o de pago) 1002/cncy.21332

AUTORES / AUTHORS: - Hooper K; Mukhtar F; Li S; Eltoum IA

INSTITUCIÓN / INSTITUTION: - Department of Pathology, University of Alabama at Birmingham, Birmingham, Alabama.

RESUMEN / SUMMARY: - BACKGROUND: Over the past decade, the standardization of error classification in anatomic pathology has become an important issue. The objective of the current study was to assess the extent of errors occurring in the cytopathologic diagnosis of neuroendocrine lesions of the pancreas, and to classify these errors and their associated harm. METHODS: Information on all cases diagnosed as a neuroendocrine neoplasm either by endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) in cytology or by surgical pathology between 2000 and 2012 was collected. Using standardized error and harm classification, the authors reviewed the cytology and surgical pathology material and evaluated the type and the cause of diagnostic errors and their impact on the patient. RESULTS: A total of 177 patients who underwent EUS-FNA were diagnosed with a neuroendocrine neoplasm either by cytology or surgical pathology. Eighty of these cases had surgical follow-up available at the study institution. Of these 80 cases, 56 had an adequate cell block and immunohistochemistry was performed. There were 14 discrepancies noted between cytologic and surgical pathologic diagnoses. There were 9 false-negative cases, consisting of 3 interpretation errors and 6 cytology sampling errors. There were 5 misclassifications, including 4 cases of solid pseudopapillary neoplasm and 1 case of neuroendocrine carcinoma (diagnosed as adenocarcinoma on cytology). There were no surgical pathology errors noted. All errors were associated with no or minor harm.

CONCLUSIONS: EUS-FNA of pancreatic neuroendocrine neoplasms has excellent diagnostic performance, with no false-positive diagnoses reported. When an adequate sample is obtained, the most significant error is misclassification, which is most often associated with solid pseudopapillary neoplasm. The harm associated with diagnostic errors is at most minor. Cancer (Cancer Cytopathol) 2013. © 2013 American Cancer Society.

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[368]

TÍTULO / TITLE: - Pancreatic and peripancreatic tuberculosis presenting as hypoechoic mass and malignancy diagnosed by ultrasound-guided fine-needle aspiration cytology.

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

REVISTA / JOURNAL: - J Cytol. 2013 Apr;30(2):130-5. doi: 10.4103/0970-9371.112658.

●● Enlace al texto completo (gratuito o de pago) 4103/0970-9371.112658

AUTORES / AUTHORS: - Rao RN; Pandey R; Rana MK; Rai P; Gupta A

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India.

RESUMEN / SUMMARY: - BACKGROUND: Pancreatic and peripancreatic tuberculosis is an extremely uncommon disease, presenting as hypoechoic mass on ultrasonography and imaging mimicking malignancy. Consequently, it represents a diagnostic challenge. AIMS: To study 14 unusual cases of pancreatic and peripancreatic tuberculosis undergoing ultrasound-/endoscopic-guided fine-needle aspiration cytology (FNAC) in the 5-year period from 2006 to 2010. MATERIALS AND METHODS: Endoscopic-guided FNAC was done in two cases, while ultrasound-guided FNAC was performed in 12 cases using 22-G needles via a percutaneous transabdominal approach. The aspirated material was quickly smeared onto glass slides, air dried, and wet fixed in 95% ethyl alcohol for subsequent Papanicolaou staining. RESULTS: All pancreatic and peripancreatic tuberculosis cases showed solid-cystic pancreatic mass. Smears showed epithelioid cell granulomas, multinucleated giant cells, mixed inflammatory cells and histiocytes against a necrotic background. The common anatomic locations were the head, peripancreatic, tail and body of the pancreas. CONCLUSIONS: Ultrasound-/endoscopic-guided FNAC is a safe, reliable and cost-effective method for preoperative diagnosis of pancreatic and peripancreatic tuberculosis. Clinical symptoms and accurate diagnostic approach by ultrasound-/endoscopic-guided FNAC of pancreatic and peripancreatic tuberculosis is needed to avoid performing redundant laparotomy. Despite its rarity, pancreatic and peripancreatic tuberculosis should be considered for differential diagnosis of pancreatic and peripancreatic cystic mass in endemic developing countries.

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[369]

TÍTULO / TITLE: - Update on phase I studies in advanced pancreatic adenocarcinoma. Hunting in darkness?

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):354-8. doi: 10.6092/1590-8577/1664.

AUTORES / AUTHORS: - Strimpakos AS; Saif MW

INSTITUCIÓN / INSTITUTION: - Tufts University School of Medicine. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - Over the last twenty years, there is a limited number of effective cytotoxic or biological agents that managed to get approval in advanced pancreatic ductal adenocarcinoma. Despite numerous trials, investments in translational research and generally in health care, the survival of pancreatic cancer patients has improved by a few only months. This disappointing reality necessitates a better understanding of the pathogenesis of this disease and the identification of targetable alterations which might lead to development of more effective drugs or better combinations. At the 2013 Annual Meeting of the American Society of Clinical Oncology, few novel agents and new therapeutic concepts, tested in phase I studies in advanced pancreatic ductal adenocarcinoma, were presented. The first notable phase I study referred to the combination of chemotherapy with local delivery of silencing RNA against the K-ras mutation G12D, in advanced pancreatic ductal adenocarcinoma, which was well tolerated and promising (Abstract #4037). The second one referred to a combination of gemcitabine with pegylated recombinant human hyaluronidase (PEGPH20), an inhibitor of hyaluronan which as a matrix glycosaminoglycan is believed to play role in the reduced drug delivery to cancer (Abstract #4010). The other notable abstract was related to an early phase study which tested the safety and toxicity of arctigenin, a traditional herbal agent found in Arctium lappa Linne, administered as an oral formulation (GMS-01) in pancreatic ductal adenocarcinoma patient resistant to standard chemotherapy (Abstract #2559). The aforementioned early phase studies open new therapeutic approaches which deserve further testing in advanced pancreatic cancer.

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[370]

TÍTULO / TITLE: - Highlights on novel imaging methods of pancreatic cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):388-90. doi: 10.6092/1590-8577/1666.

AUTORES / AUTHORS: - Krishnamoorthy SK; Hayim M; Vestal T; Saif MW

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Columbia University. New York, NY, USA. sk3552@columbia.edu.

RESUMEN / SUMMARY: - Pancreatic cancer is the fourth leading cause of cancer deaths. Since the majority of patients present with incurable metastatic disease, novel imaging methods are needed to identify pancreatic cancer and assess

response to therapy. Research presented at the 2013 American Society of Oncology (ASCO) Annual Meeting provided insight into potential imaging methods. We discuss Abstracts #4049, #TPS4144, #TPS4146, and #E15069 in this paper.

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[371]

TÍTULO / TITLE: - iTRAQ-based quantitative proteomics reveals myoferlin as a novel prognostic predictor in pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - J Proteomics. 2013 Jul 12. pii: S1874-3919(13)00380-1. doi: 10.1016/j.jprot.2013.06.032.

●● Enlace al texto completo (gratuito o de pago) 1016/j.jprot.2013.06.032

AUTORES / AUTHORS: - Wang WS; Liu LX; Zhang W; Liu XH; Yang PY; Lou WH; Jin DY; Wang XL

INSTITUCIÓN / INSTITUTION: - Department of Interventional Radiology, First Affiliated Hospital, Soochow University, Suzhou 215006, China; Department of Interventional Radiology, Zhongshan Hospital, Fudan University, Shanghai 200032, China.

RESUMEN / SUMMARY: - Histological differentiation is a major pathological parameter associated with poor prognosis in patients with pancreatic adenocarcinoma (PAC) and the molecular signature underlying PAC differentiation may involve key proteins potentially affecting the malignant characters of PAC. We aimed to identify the proteins which could be implicated in PAC prognosis. We used isobaric tags for relative and absolute quantitation (iTRAQ) coupled with two-dimensional liquid chromatography-tandem mass spectrometry to compare protein expression in PAC tissues with different degrees of histological differentiation. A total of 1623 proteins were repeatedly identified by performing the iTRAQ-based experiments twice. Of these, 15 proteins were differentially expressed according to our defined criteria. Myoferlin (MYOF) was selected to validate the proteomic results by western blotting. Immunohistochemistry in a further 154 PAC cases revealed that myoferlin significantly correlated with the degree of histological differentiation (P=0.004), and univariate and multivariate analyses indicated that MYOF is an independent prognostic factor for survival (hazard ratio, 1.540; 95% confidence interval, 1.061-2.234; P=0.023) of patients with PAC after curative surgery. RNA interference-mediated knockdown of MYOF alleviated malignant phenotypes of both primary and metastatic PAC cell lines in vitro and in vivo. Thus, ITRAQ-based quantitative proteomics revealed the prognostic value of MYOF in PAC. BIOLOGICAL SIGNIFICANCE: Our results provide the possibility of novel strategies for pancreatic adenocarcinoma management.

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[372]

TÍTULO / TITLE: - Prognostic Role of Pancreatic Metastases From Renal Cell Carcinoma: Results From an Italian Center.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Clin Genitourin Cancer. 2013 Jun 19. pii: S1558-7673(13)00083-9. doi: 10.1016/j.clgc.2013.04.022.
●● Enlace al texto completo (gratuito o de pago) 1016/j.clgc.2013.04.022
AUTORES / AUTHORS: - Grassi P; Verzoni E; Mariani L; De Braud F; Coppa J; Mazzaferro V; Procopio G
INSTITUCIÓN / INSTITUTION: - Medical Oncology Unit 1, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy.
RESUMEN / SUMMARY: - BACKGROUND: Pancreatic metastasis accounts for 2% to 11% of all mRCC cases. The prognostic value of pancreatic metastases in the era of TTs is unclear. We evaluated outcomes in a cohort of mRCC patients with pancreatic metastases (PmRCC) who were treated with TTs. PATIENTS AND METHODS: We retrospectively reviewed the records of 354 mRCC patients treated at our institute between January 2005 and June 2012. Differences in terms of OS between this unselected cohort of mRCC patients and a subgroup of patients with PmRCC were investigated. Kaplan-Meier and log-rank test methods were used to evaluate OS. RESULTS: In total, 24 PmRCC (7%) patients were identified, and were compared with a cohort of 330 mRCC patients with metastasis at other sites. Pancreatic metastases were synchronous in 3 patients, and they were metachronous in 11 patients. Surgical resection of pancreatic metastases was performed in 2 (8%) patients. At a maximum follow-up of 89 months (median, 51 months), median OS was 39 months in PmRCC patients, vs. 23 months in the mRCC patient group (P = .0004). CONCLUSION: Among mRCC patients treated with TTs, the presence of pancreatic metastasis seems to be associated with a longer survival than the presence of metastasis at other sites.

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[373]
TÍTULO / TITLE: - Prognostic factors in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):322-4. doi: 10.6092/1590-8577/1644.
AUTORES / AUTHORS: - Oikonomopoulos GM; Syrigos KN; Saif MW
INSTITUCIÓN / INSTITUTION: - Second Oncology Department, St. Savvas Anticancer Hospital. Athens, Greece. goik77@yahoo.com.
RESUMEN / SUMMARY: - Pancreatic cancer is a frequent and lethal disease ranking fourth as a cause of cancer-related death in Western countries. There are patients, though, who respond well to chemotherapy and have a prolonged survival. There is an effort towards identification of specific characteristics of these tumor cells in order to identify those patients who will benefit from chemotherapy and use them as prognostic or predictive factors. This review is an update on the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting regarding the most important developments in this field for pancreatic

cancer, as they were reported in Abstracts #4006, #4016, #4046, and #4060 and a discussion is presented about their application in clinical praxis.

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[374]

TÍTULO / TITLE: - Accuracy of Multi-Detector Computed Tomography, Fluorodeoxyglucose Positron Emission Tomography-CT, and CA 19-9 Levels in Detecting Recurrent Pancreatic Adenocarcinoma.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 11;14(4):466-8. doi: 10.6092/1590-8577/1529.

AUTORES / AUTHORS: - Hamidian Jahromi A; Sangster G; Zibari G; Martin B; Chu Q; Takalkar A; Shi R; Shokouh-Amiri H

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Louisiana State University. Shreveport, LA, USA. alirezahamidian@yahoo.com.

RESUMEN / SUMMARY: - CONTEXT: We compared the accuracy of fluorodeoxyglucose positron emission tomography-CT (FDG-PET-CT), multi-detector computed tomography (MDCT) and CA 19-9 levels in detecting pancreatic cancer recurrence in patients with resected CA 19-9 positive pancreatic adenocarcinomas. METHODS: We retrospectively evaluated 122 patients with pancreatic adenocarcinomas who underwent surgical resection of the tumor between January 2002 and December 2011. Twenty-five patients had MDCT, FDG-PET-CT and CA 19-9 levels performed no less than six weeks post-operation and within 8 weeks of each other for detection of tumor recurrence. Of these, 20 patients had high pre-operative CA 19-9 levels that dropped to a normal level postoperatively which will be the focus of this study. The sensitivity, specificity, positive and negative predictive value (PPV, NPV), and accuracy of MDCT, FDG-PET-CT, and CA 19-9 in detecting recurrence were compared. RESULTS: Operations performed included pyloric sparing pancreaticoduodenectomy (n=9), pancreaticoduodenectomy (n=7), distal pancreatectomy (n=3) and total pancreatectomy (n=1). Three patients had no recurrence, but local recurrence and distant metastasis were seen in 8 (40%) and 12 (60%) patients, respectively. In our study, sensitivity, specificity, PPV, NPV and diagnostic effectiveness (accuracy) were: 82%, 100%, 100%, 50%, 85% for MDCT; 82%, 100%, 100%, 50%, 85% for FDG-PET-CT and 94%, 100%, 100%, 75%, 95% for CA 19-9. The difference in recurrence detection accuracy of the tests was not statistically significant. A combination of CA 19-9 with MDCT or FDG-PET-CT was 100% accurate in detecting cancer recurrence in our patients. CONCLUSION: Our data suggests that CA 19-9 levels can be used reliably to detect recurrent pancreatic adenocarcinomas in patients with CA 19-9-positive primary tumors. Combination of CA 19-9 with MDCT or FDG-PET-CT is potentially the most accurate approach in detecting pancreatic cancer recurrence.

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[375]

TÍTULO / TITLE: - An iPSC Line from Human Pancreatic Ductal Adenocarcinoma Undergoes Early to Invasive Stages of Pancreatic Cancer Progression.

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

REVISTA / JOURNAL: - Cell Rep. 2013 Jun 27;3(6):2088-99. doi: 10.1016/j.celrep.2013.05.036. Epub 2013 Jun 20.

●● Enlace al texto completo (gratuito o de pago) 1016/j.celrep.2013.05.036

AUTORES / AUTHORS: - Kim J; Hoffman JP; Alpaugh RK; Rhimm AD; Reichert M; Stanger BZ; Furth EE; Sepulveda AR; Yuan CX; Won KJ; Donahue G; Sands J; Gumbs AA; Zaret KS

INSTITUCIÓN / INSTITUTION: - Institute for Regenerative Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104-5157, USA; Department of Cell and Developmental Biology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104-5157, USA; Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104-5157, USA.

RESUMEN / SUMMARY: - Pancreatic ductal adenocarcinoma (PDAC) carries a dismal prognosis and lacks a human cell model of early disease progression. When human PDAC cells are injected into immunodeficient mice, they generate advanced-stage cancer. We hypothesized that if human PDAC cells were converted to pluripotency and then allowed to differentiate back into pancreatic tissue, they might undergo early stages of cancer. Although most induced pluripotent stem cell (iPSC) lines were not of the expected cancer genotype, one PDAC line, 10-22 cells, when injected into immunodeficient mice, generated pancreatic intraepithelial neoplasia (PanIN) precursors to PDAC that progressed to the invasive stage. The PanIN-like cells secrete or release proteins from many genes that are known to be expressed in human pancreatic cancer progression and that predicted an HNF4alpha network in intermediate-stage lesions. Thus, rare events allow iPSC technology to provide a live human cell model of early pancreatic cancer and insights into disease progression.

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[376]

TÍTULO / TITLE: - Pancreatic cancer: Slow progression in the early stages.

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

REVISTA / JOURNAL: - Int J Surg Case Rep. 2013;4(8):693-6. doi: 10.1016/j.ijscr.2013.04.040. Epub 2013 May 22.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ijscr.2013.04.040

AUTORES / AUTHORS: - Nakamura T; Masuda K; Harada S; Akioka K; Sako H

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Omihachiman Medical Community Center, Tsuchida-cho 1379, Omihachiman, Shiga, Japan. Electronic address: tsukasa@koto.kpu-m.ac.jp.

RESUMEN / SUMMARY: - INTRODUCTION: The rates of pancreatic cancer development in the early stages of growth remain unclear; but it is generally believed that they demonstrate a rapid degree of progression. There is

evidence to suggest that pancreatic cancers measuring less than 1cm demonstrate better survival rates, hence it is clear that detecting pancreatic cancers less than 1cm in size is of paramount importance. However, to date, there has been no scientifically adequate research to show the growth rate of small pancreatic cancers less than 1cm in the early stages. PRESENTATION OF CASE: We present the case of a 65-year-old woman whose small pancreatic cancer possibly demonstrated a slow progressive rate as it grew to an invasive carcinoma measuring 1cm diameter from over the 29 months. DISCUSSION: It is reasonable to assume that the progression of some pancreatic cancers until 1cm size, can take up to 29 months. During this silent period, it is crucial to detect such a small pancreatic cancer by means of the initial US and subsequent EUS and ERCP. It is clear, therefore, that clinicians have to be aware of the growth rate of small pancreatic cancers and in particular high risk patients should be encouraged to monitor size of the main pancreatic duct by means of US on regular basis. CONCLUSION: This could give better outcomes for pancreatic cancer patients. Hopefully, by detecting these lethal, pancreatic cancers in their early stages, it will give us an extension of time to perform effective therapies.

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[377]

TÍTULO / TITLE: - The rise and fall of cancer mortality in the USA: why does pancreatic cancer not follow the trend?

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

REVISTA / JOURNAL: - Future Oncol. 2013 Jul;9(7):917-9. doi: 10.2217/fon.13.76.

●● Enlace al texto completo (gratuito o de pago) 2217/fon.13.76

AUTORES / AUTHORS: - Ma J; Jemal A

INSTITUCIÓN / INSTITUTION: - Surveillance & Health Services Research Program, American Cancer Society, 250 Williams Street, Atlanta, GA 30303, USA.

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[378]

TÍTULO / TITLE: - Increase in PI3K signalling mimics mutated-Kras induction of pancreatic cancer.

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

REVISTA / JOURNAL: - Clin Res Hepatol Gastroenterol. 2013 Jun 6. pii: S2210-7401(13)00093-4. doi: 10.1016/j.clinre.2013.04.006.

●● Enlace al texto completo (gratuito o de pago) 1016/j.clinre.2013.04.006

AUTORES / AUTHORS: - Baer R; Pyronnet S; Guillermet-Guibert J

INSTITUCIÓN / INSTITUTION: - Inserm UMR 1037, universite de Toulouse III, centre de recherche en cancerologie de Toulouse (CRCT), CHU de Rangueil, BP 84225, 31432 Toulouse, France.

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[379]

TÍTULO / TITLE: - Utilizing endoscopic ultrasound-guided fine needle aspiration in identifying molecular targets for pancreatic cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):316-7. doi: 10.6092/1590-8577/1642.

AUTORES / AUTHORS: - Ogbonna OH; Saif MW

INSTITUCIÓN / INSTITUTION: - Tufts University School of Medicine. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - Pancreatic cancer remains a devastating disease, with poor survival rates and high recurrence rates with current treatment regimens. Over the years we have come to understand the complex biology of this cancer, involving cross-talking signaling pathways that proffers resistance to current therapy. Several molecularly targeted agents remain in development. At the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting, an abstract (#4051) was presented which explored using endoscopic ultrasound-guided fine needle aspiration of pancreatic cancer tissue to identify molecular targets, and argued for the feasibility of personalizing pancreatic cancer therapy based on the activated molecular pathways identified. We summarize their findings and discuss the possibility of utilizing this model to obtain a better understanding of pancreatic cancer at each stage of its metamorphosis and target therapy at these different levels.

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[380]

TÍTULO / TITLE: - Radiotherapy prolongs biliary metal stent patency in malignant pancreatobiliary obstructions.

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

REVISTA / JOURNAL: - Gut Liver. 2013 Jul;7(4):480-5. doi: 10.5009/gnl.2013.7.4.480. Epub 2013 Jun 11.

●● Enlace al texto completo (gratuito o de pago) 5009/gnl.2013.7.4.480

AUTORES / AUTHORS: - Park S; Park JY; Bang S; Park SW; Chung JB; 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: Biliary stenting is the most effective decompressive method for treating malignant biliary obstructive jaundice. Although the main cause of stent occlusion is tumor growth, few studies have investigated whether stent patency is affected by the combination of cancer-treatment modalities. The aim of this study was to evaluate the effects of local radiotherapy on metal-stent patency in patients with malignant biliary obstruction. METHODS: Patients who underwent self-expandable biliary metallic stenting for malignant biliary obstruction from 1999 to 2007 were included. Forty patients received chemotherapy and radiation therapy (radiation group, RG), and 31 patients received only chemotherapy (nonradiation group,

NRG). RESULTS: The cumulative median stent patency was significantly longer in the RG than in the NRG (17.7 months; 95% confidence interval [CI], 1.8 to 33.6 months vs 8.7 months; 95% CI, 4.9 to 12.5 months; p=0.025). Stent occlusion caused by tumor growth or stent migration occurred in two (5%) and three (7.5%) cases in the RG and in six (19.3%) and two (6.5%) cases in the NRG, respectively. CONCLUSIONS: The patency of biliary metal stents in pancreatobiliary cancer patients who receive chemoradiation therapy is significantly longer than that in patients who do not receive radiotherapy, which suggests that local cancer control significantly affects stent patency.

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[381]

TÍTULO / TITLE: - Tumor markers in pancreatic cancer: 2013.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):318-21. doi: 10.6092/1590-8577/1653.

AUTORES / AUTHORS: - Shah UA; Saif MW

INSTITUCIÓN / INSTITUTION: - Tufts Medical Center. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - Amongst the tumor markers for pancreatic cancer CA 19-9 is being used most widely and newer clinically useful applications of this tumor marker are being researched. We will discuss four abstracts presented at the American Society of Clinical Oncology (ASCO) Annual Meeting which contribute to expanding the application of CA 19-9 measurement (Abstracts #4042, #4058, #e15082, #e15146).

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[382]

TÍTULO / TITLE: - Aggressive secondary surgery for local recurrence of pancreatic cancer.

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

REVISTA / JOURNAL: - British Medical J (BMJ). %8?(3k+]3s http://bmj.com/search.dtl ●● British Medical J. (BMJ): <> Case Rep. 2013 Jun 16;2013. pii: bcr2013009914. doi: 10.1136/bcr-2013-009914.

●● Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-009914

AUTORES / AUTHORS: - Shimoike N; Fujikawa T; Maekawa H; Tanaka A

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Kokura Memorial Hospital, Kitakyushu, Fukuoka, Japan.

RESUMEN / SUMMARY: - We report two cases of locally recurrent pancreatic cancer treated with repeated resection. In both cases, local recurrence was found in the cut end of the remnant pancreas after initial pancreatic resection, and total remnant pancreatectomy was performed. The postoperative course was uneventful and long-term survival was achieved. Aggressive repeated surgical resection could improve the prognosis of selected patients who are suffering from local recurrence of pancreatic cancer, and can be considered as a treatment option.

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[383]

TÍTULO / TITLE: - In vitro evaluation of photon and raster-scanned carbon ion radiotherapy in combination with gemcitabine in pancreatic cancer cell lines.

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

REVISTA / JOURNAL: - J Radiat Res. 2013 Jul;54 Suppl 1:i113-i119. doi: 10.1093/jrr/rrt052.

●● Enlace al texto completo (gratuito o de pago) 1093/jrr/rrt052

AUTORES / AUTHORS: - El Shafie RA; Habermehl D; Rieken S; Mairani A; Orschiedt L; Brons S; Haberer T; Weber KJ; Debus J; Combs SE

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Heidelberg, Im Neuenheimer Feld 400, 69120 Heidelberg, Germany.

RESUMEN / SUMMARY: - Background: Pancreatic cancer is the fourth leading cause of cancer deaths, being responsible for 6% of all cancer-related deaths. Conventional radiotherapy with or without additional chemotherapy has been applied in the past in the context of neoadjuvant or adjuvant therapy concepts with only modest results, however new radiation modalities, such as particle therapy with promising physical and biological characteristics, present an alternative treatment option for patients with pancreatic cancer. Up until now the raster scanning technique employed at our institution for the application of carbon ions has been unique, and no radiobiological data using pancreatic cancer cells has been available yet. The aim of this study was to evaluate cytotoxic effects that can be achieved by treating pancreatic cancer cell lines with combinations of X-rays and gemcitabine, or alternatively with carbon ion irradiation and gemcitabine, respectively. Materials and Methods: Human pancreatic cancer cell lines AsPC-1, BxPC-3 and Panc-1 were irradiated with photons and carbon ions at various doses and treated with gemcitabine. Photon irradiation was applied with a biological cabin X-ray irradiator, and carbon ion irradiation was applied with an extended Bragg peak (linear energy transfer (LET) 103 keV/mum) using the raster scanning technique at the Heidelberg Ion Therapy Center (HIT). Responsiveness of pancreatic cancer cells to the treatment was measured by clonogenic survival. Clonogenic survival curves were then compared to predicted curves that were calculated employing the local effect model (LEM). Results: Cell survival curves were calculated from the surviving fractions of each combination experiment and compared to a drug control that was only irradiated with X-rays or carbon ions, without application of gemcitabine. In terms of cytotoxicity, additive effects were achieved for the cell lines Panc-1 and BxPC-3, and a slight radiosensitizing effect was observed for AsPC-1. Relative biological effectiveness (RBE) of carbon ion irradiation ranged from 1.5-4.5 depending on survival level and dose. Sensitizer enhancement ratio (SER) values calculated at 10% cell survival ranged from 1.24-1.66, depending on cell line, gemcitabine dose and irradiation modality. Experimentally ascertained survival curves matched those predicted by LEM-calculation. Conclusion: Our experiments have shown a combined treatment of

irradiation and chemotherapy with gemcitabine to be a good means of achieving additive cytotoxic effects on pancreatic cancer cell lines. The data generated in this study will serve as radiobiological basis for further preclinical and clinical studies.

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[384]

TÍTULO / TITLE: - Beta-adrenergic signaling in the development and progression of pulmonary and pancreatic adenocarcinoma.

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

REVISTA / JOURNAL: - Curr Cancer Ther Rev. 2012 May 1;8(2):116-127.

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

2174/157339412800675351

AUTORES / AUTHORS: - Schuller HM; Al-Wadei HA

INSTITUCIÓN / INSTITUTION: - Experimental Oncology Laboratory, Department of Biomedical & Diagnostic Sciences, College of Veterinary Medicine, University of Tennesse, Knoxville, TN, USA.

RESUMEN / SUMMARY: - Small airway epithelial cells from, which most pulmonary adenocarcinomas (PACs) derive, and pancreatic duct epithelia, from which pancreatic ductal adenocarcinomas (PDACs) originate, share the ability to synthesize and release bicarbonate. This activity is stimulated in both cell types by the alpha7nicotinic acetylcholine receptor (alpha7nAChR)-mediated release of noradrenaline and adrenaline, which in turn activate beta-adrenergic receptor (beta-AR) signaling, leading to the cAMP-dependent release of bicarbonate. The same signaling pathway also stimulates a complex network of intracellular signaling cascades which regulate the proliferation, migration, angiogenesis and apoptosis of PAC and PDAC cells. The amino acid neurotransmitter gamma-aminobutyric acid (GABA) serves as the physiological inhibitor of this cancer stimulating network by blocking the activation of adenylyl cyclase. This review summarizes experimental, epidemiological and clinical data that have identified risk factors for PAC and PDAC such as smoking, alcoholism, chronic non neoplastic diseases and their treatments as well as psychological stress and analyzes how these factors increase the cancer-stimulating effects of this regulatory cascade in PAC and PDAC. This analysis identifies the careful maintenance of balanced levels in stimulatory stress neurotransmitters and inhibitory GABA as a key factor for the prevention of PDAC and suggests the marker-guided use of beta-blockers, GABA or GABA-B receptor agonists as well as psychotherapeutic or pharmacological stress reduction as important tools that may render currently ineffective cancer intervention of PAC and PDAC more successful.

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[385]

TÍTULO / TITLE: - Blood group determinates incidence for pancreatic cancer in Germany.

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

REVISTA / JOURNAL: - Front Physiol. 2013 May 24;4:118. doi: 10.3389/fphys.2013.00118. Print 2013.

●● Enlace al texto completo (gratuito o de pago) 3389/fphys.2013.00118

AUTORES / AUTHORS: - Pelzer U; Klein F; Bahra M; Sinn M; Dorken B; Neuhaus P; Meyer O; Riess H

INSTITUCIÓN / INSTITUTION: - Department of Hematology/Oncology, Comprehensive Cancer Center, Charite - Universitatsmedizin Berlin Berlin, Germany.

RESUMEN / SUMMARY: - Background: Genetic risk factors for sporadic pancreatic cancer are largely unknown but actually under high exposure. Findings of correlations between the AB0 blood group system (Chromosome 9q34,1-q34,2) and the risk of pancreatic cancer (PC) in patients from Asia, America and south Europe have already been published. So far it is unclear, whether this correlation between blood group an PC incidence can be found in German patients as well. Methods: One hundred and sixty-six patients who underwent a resection of PC were evaluated in a period between 2000 and 2010. Blood group reference distribution for the German population is given as: 0: 41%; A: 43%; B: 11%; AB: 5%; Rhesus positive: 85%; Rhesus negative: 15%. Analyses were done using the non-parametric Chi(2)-test (p-value two sided; SPSS 19.0). Results: Median age was 62 (34-82) years. Gender: female 73/44%; male: 93/56%. Observed blood group proportions: 0: 43 (25.9%)/A: 94 (56.6%)/B: 16 (9.6%)/AB: 13 (7.8%)/Rhesus positive: 131 (78.9%)/negative: 35 (21.1%). We detected a significant difference to the German reference distribution of the AB0 system (Chi(2) 19.34, df 3, $p < 0.001$). Rhesus factor has no impact on AB0-distribution (Chi(2) 4.13, df 3, $p = 0.25$), but differs significantly from reference distribution-probably due to initial AB0-variation (Chi(2) 4.82, df 1, $p = 0.028$). The odds ratio for blood group A is 2.01 and for blood group 0 is 0.5. Conclusions: The incidence of PC in the German cohort is highly associated with the AB0-system as well. More patients with blood group A suffer from PC ($p < 0.001$) whereas blood group 0 was less frequent in patients with PC ($p < 0.001$). Thus, our findings support the results from other non-German surveys. The causal trigger points of this carcinogenesis correlation are still not known.

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[386]

TÍTULO / TITLE: - Reconstruction of portal vein and superior mesenteric vein after extensive resection for pancreatic cancer.

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

REVISTA / JOURNAL: - J Korean Surg Soc. 2013 Jun;84(6):346-52. doi: 10.4174/jkss.2013.84.6.346. Epub 2013 May 28.

●● Enlace al texto completo (gratuito o de pago) 4174/jkss.2013.84.6.346

AUTORES / AUTHORS: - Kim SM; Min SK; Park D; Min SI; Jang JY; Kim SW; Ha J; Kim SJ

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Seoul National University College of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - PURPOSE: Tumor invasion to the portal vein (PV) or superior mesenteric vein (SMV) can be encountered during the surgery for pancreatic cancer. Venous reconstruction is required, but the optimal surgical methods and conduits remain in controversies. METHODS: From January 2007 to July 2012, 16 venous reconstructions were performed during surgery for pancreatic cancer in 14 patients. We analyzed the methods, conduits, graft patency, and patient survival. RESULTS: The involved veins were 14 SMVs and 2 PVs. The operative methods included resection and end-to-end anastomosis in 7 patients, wedge resection with venoplasty in 2 patients, bovine patch repair in 3 patients, and interposition graft with bovine patch in 1 patient. In one patient with a failed interposition graft with great saphenous vein (GSV), the SMV was reconstructed with a prosthetic interposition graft, which was revised with a spiral graft of GSV. Vascular morbidity occurred in 4 cases; occlusion of an interposition graft with GSV or polytetrafluoroethylene, segmental thrombosis and stenosis of the SMV after end-to-end anastomosis. Patency was maintained in patients with bovine patch angioplasty and spiral vein grafts. With mean follow-up of 9.8 months, the 6- and 12-month death-censored graft survival rates were both 81.3%. CONCLUSION: Many of the involved vein segments were repaired primarily. When tension-free anastomosis is impossible, the spiral grafts with GSV or bovine patch grafts are good options to overcome the size mismatch between autologous vein graft and portomesenteric veins. Further follow-up of these patients is needed to demonstrate long-term patency.

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[387]

TÍTULO / TITLE: - A self antigen reopens the games in pancreatic cancer.

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

REVISTA / JOURNAL: - Oncoimmunology. 2013 Jun 1;2(6):e24384. Epub 2013 May 10.

●● Enlace al texto completo (gratuito o de pago) 4161/onci.24384

AUTORES / AUTHORS: - Cappello P; Novelli F

INSTITUCIÓN / INSTITUTION: - Center for Experimental Research and Medical Studies (CERMS); Citta della Salute e della Scienza di Torino; University of Torino; Torino, Italy ; Department of Molecular Biotechnology and Health Sciences; University of Torino; Torino, Italy.

RESUMEN / SUMMARY: - We have recently demonstrated that the administration of a plasmid coding for alpha-enolase can elicit robust immune responses in genetically engineered mice that spontaneously develop pancreatic cancer, resulting in a significant improvement of their survival. This approach provides a springboard for the elaboration of new forms of immunotherapy for pancreatic cancer.

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[388]
TÍTULO / TITLE: - HuR is a post-transcriptional regulator of core metabolic enzymes in pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - RNA Biol. 2013 Jun 13;10(8).
AUTORES / AUTHORS: - Burkhart RA; Pineda DM; Chand SN; Romeo C; Londin ER; Karoly ED; Cozzitorto JA; Rigoutsos I; Yeo CJ; Brody JR; Winter JM
INSTITUCIÓN / INSTITUTION: - Department of Surgery; Jefferson Pancreas, Biliary and Related Cancer Center; Philadelphia, PA USA.
RESUMEN / SUMMARY: - Cancer cell metabolism differs from normal cells, yet the regulatory mechanisms responsible for these differences are incompletely understood, particularly in response to acute changes in the tumor microenvironment. HuR, an RNA-binding protein, acts under acute stress to regulate core signaling pathways in cancer through post-transcriptional regulation of mRNA targets. We demonstrate that HuR regulates the metabolic phenotype in pancreatic cancer cells and is critical for survival under acute glucose deprivation. Using three pancreatic cancer cell line models, HuR-proficient cells demonstrated superior survival under glucose deprivation when compared with isogenic cells with siRNA-silencing of HuR expression (HuR-deficient cells). We found that HuR-proficient cells utilized less glucose, but produced greater lactate, as compared with HuR-deficient cells. Acute glucose deprivation was found to act as a potent stimulus for HuR translocation from the nucleus to the cytoplasm, where HuR stabilizes its mRNA targets. We performed a gene expression array on ribonucleoprotein-immunoprecipitated mRNAs bound to HuR and identified 11 novel HuR target transcripts that encode enzymes central to glucose metabolism. Three (GPI, PRPS2 and IDH1) were selected for validation studies, and confirmed as bona fide HuR targets. These findings establish HuR as a critical regulator of pancreatic cancer cell metabolism and survival under acute glucose deprivation. Further explorations into HuR's role in cancer cell metabolism should uncover novel therapeutic targets that are critical for cancer cell survival in a metabolically compromised tumor microenvironment.

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[389]
TÍTULO / TITLE: - Pancreatic cancers rely on a novel glutamine metabolism pathway to maintain redox balance.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Cell Cycle. 2013 Jul 1;12(13):1987-8. doi: 10.4161/cc.25307. Epub 2013 Jun 10.
●● Enlace al texto completo (gratuito o de pago) 4161/cc.25307
AUTORES / AUTHORS: - Lyssiotis CA; Son J; Cantley LC; Kimmelman AC
INSTITUCIÓN / INSTITUTION: - Department of Medicine; Weill Cornell Medical College; New York, NY USA.

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[390]
TÍTULO / TITLE: - New developments in the management of borderline resectable pancreatic cancers.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):334-6. doi: 10.6092/1590-8577/1681.
AUTORES / AUTHORS: - Goodman MD; McPartland S; Huber K; Saif MW
INSTITUCIÓN / INSTITUTION: - Tufts Medical Center. Boston, MA, USA. mgoodman@tuftsmedicalcenter.org.
RESUMEN / SUMMARY: - There remains great variability in the treatment for patients with borderline resectable pancreatic head cancers. Whether surgery should be attempted or neoadjuvant therapy consisting of chemoradiation or chemotherapy alone is at some debate. Each neoadjuvant regimen does show efficacy but there is no clear consensus which would be most beneficial. We will discuss three abstracts (#4043, #4057, #e15082) that were presented in the 2013 ASCO Annual Meeting that will discuss neoadjuvant therapies and how they are related to getting an R0 resection.

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[391]
TÍTULO / TITLE: - Basic research: Wnt signalling required for pancreatic carcinogenesis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Nat Rev Clin Oncol. 2013 Aug;10(8):428. doi: 10.1038/nrclinonc.2013.116. Epub 2013 Jul 2.
●● Enlace al texto completo (gratuito o de pago) 1038/nrclinonc.2013.116

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[392]
TÍTULO / TITLE: - SBRT in unresectable advanced pancreatic cancer: preliminary results of a mono-institutional experience.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Radiat Oncol. 2013 Jun 21;8(1):148.
●● Enlace al texto completo (gratuito o de pago) 1186/1748-717X-8-148
AUTORES / AUTHORS: - Tozzi A; Comito T; Alongi F; Navarria P; Iftode C; Mancosu P; Reggiori G; Clerici E; Rimassa L; Zerbi A; Fogliata A; Cozzi L; Tomatis S; Scorsetti M
RESUMEN / SUMMARY: - BACKGROUND: To assess the efficacy and safety of stereotactic body radiotherapy (SBRT) in patients with either unresectable locally advanced pancreatic adenocarcinoma or by locally recurrent disease after surgery. METHODS: Between January 2010 and October 2011, 30 patients with unresectable or recurrent pancreatic adenocarcinoma underwent exclusive SBRT. Twenty-one patients (70%) presented with unresectable locally advanced disease and 9 patients (30%) showed local recurrence after surgery. No patients had metastatic disease. Gemcitabine-based chemotherapy was

administered to all patients before SBRT. Prescription dose was 45Gy in 6 daily fractions of 7.5Gy. SBRT was delivered using the volumetric modulated arc therapy (VMAT) by RapidArc. Primary end-point of this study was freedom from local progression (FFLP), secondary end-points were overall survival (OS), progression free survival (PFS) and toxicity. RESULTS: Median Clinical Target Volume (CTV) was 25.6 cm3 (3.2-78.8 cm3) and median Planning Target Volume (PTV) was 70.9 cm3 (20.4- 205.2 cm3). The prescription dose was delivered in 25 patients (83%), in 5 patients (17%) it was reduced to 36Gy in 6 fractions not to exceed the dose constraints of organs at risk (OARs). Median follow-up was 11 months (2--28 months). FFLP was 91% at 6 months, 85% at median follow-up and 77% at 1 and 2 years. For the group with prescription dose of 45Gy, FFLP was 96% at 1 and 2 years. The median PFS was 8 months. The OS was 47% at 1 year and median OS was 11 months. At the end of the follow-up, 9 patients (32%) were alive and 4 (14%) were free from progression. No patients experienced G >= 3 acute toxicity. CONCLUSIONS: Our preliminary results show that SBRT can obtain a satisfactory local control rate for unresectable locally advanced and recurrent pancreatic adenocarcinoma. This fractionation schedule is feasible, and no G >= 3 toxicity was observed. SBRT is an effective emerging technique in the multi-modality treatment of locally advanced pancreatic tumors.

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[393]

TÍTULO / TITLE: - Primary human non-small cell lung and pancreatic tumorgraft models—utility and applications in drug discovery and tumor biology.

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

REVISTA / JOURNAL: - Curr Protoc Pharmacol. 2013 Jun;Chapter 14:Unit 14.26. doi: 10.1002/0471141755.ph1426s61.

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

1002/0471141755.ph1426s61

AUTORES / AUTHORS: - Calles A; Rubio-Viqueira B; Hidalgo M

INSTITUCIÓN / INSTITUTION: - Clinical Research Programme, Spanish National Cancer Research Centre-CNIO, Madrid, España.

RESUMEN / SUMMARY: - The number of therapeutic options for lung and pancreatic cancer is increasing because of the identification of new druggable molecular targets and development of new drug combinations. Reproducible, biologically relevant in vivo pre-clinical models are critical for this effort. The generation of patient-derived tumor xenografts has proven useful for integrating drug screening with biomarker discovery, discovering fundamental information in tumor biology, prioritizing drugs for clinical investigation, and personalizing treatments for these tumors. The protocol described in this unit details how to establish a direct in vivo subcutaneous primary tumorgraft and maintenance passages. The predictive value of a tumorgraft platform to guide personalized medicine is illustrated with the case of a patient with refractory advanced non-small cell lung cancer (NSCLC). The outcome of a patient for whom their own

pancreatic tumorgraft revealed a remarkable sensitivity to mitomycin C based on a PALB2 mutation is also detailed.

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[394]

TÍTULO / TITLE: - alpha-Mangostin suppresses lipopolysaccharide-induced invasion by inhibiting matrix metalloproteinase-2/9 and increasing E-cadherin expression through extracellular signal-regulated kinase signaling in pancreatic cancer cells.

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

REVISTA / JOURNAL: - Oncol Lett. 2013 Jun;5(6):1958-1964. Epub 2013 Apr 4.

●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1290

AUTORES / AUTHORS: - Yuan J; Wu Y; Lu G

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, The Affiliated Hospital of Yan'an University, Yan'an, Shaanxi 716000;

RESUMEN / SUMMARY: - Invasion and metastasis are major factors in the poor prognosis of pancreatic cancer, which remains one of the most aggressive and lethal diseases worldwide. alpha-mangostin, a major xanthone compound identified in the pericarp of mangosteen (Garcinia mangostana, Linn; GML), possesses unique biological activities, including antioxidant, antitumor and anti-inflammatory effects. Whether alpha-mangostin is able to inhibit the invasive ability of pancreatic cancer cells has not been elucidated. In the present study, alpha-mangostin was shown to inhibit the invasive ability of the pancreatic cancer cell lines MIAPaCa-2 and BxPC-3. The results showed that alpha-mangostin inhibited the growth of the pancreatic cancer cells in a dose- and time-dependent manner. At concentrations of <5 muM, alpha-mangostin had no significant effects on cytotoxicity, but significantly inhibited the invasion and migration of pancreatic cancer cells and the expression of matrix metalloproteinase (MMP)-2 and MMP-9, while increasing the expression of E-cadherin. The present data also showed that alpha-mangostin exerted an inhibitory effect on the phosphorylation of extracellular-signal-regulated kinase (ERK). Furthermore, the reduction of ERK phosphorylation by small interfering RNA (siRNA) potentiated the effect of alpha-mangostin. Taken together, the data suggest that alpha-mangostin inhibited the invasion and metastasis of pancreatic cancer cells by reducing MMP-2 and MMP-9 expression, increasing E-cadherin expression and suppressing the ERK signaling pathway. The present study suggests that alpha-mangostin may be a promising agent against pancreatic cancer.

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[395]

TÍTULO / TITLE: - Recurrence of non-invasive intraductal papillary municious neoplasm seven years following total pancreatectomy.

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

REVISTA / JOURNAL: - Int J Surg Case Rep. 2013 May 28;4(9):789-791. doi: 10.1016/j.ijscr.2013.05.009.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ijscr.2013.05.009

AUTORES / AUTHORS: - Dejean NM; Dumitra S; Barkun JS

INSTITUCIÓN / INSTITUTION: - Resident in Internal Medicine, Sherbrooke University, 12125 Desencalves, Montreal, QC, Canada H3M 2W2. Electronic address: nayima.c@gmail.com.

RESUMEN / SUMMARY: - INTRODUCTION: Intraductal papillary mucinous neoplasm is an increasingly recognized disease with varying premalignant potential and unclear incidence, characterized by a mucin-producing epithelium and dilation of the pancreatic duct. PRESENTATION OF CASE: We present the first documented case of distant intestinal intraductal papillary mucinous neoplasm recurrence following total pancreatectomy for side-branch non-invasive borderline malignant intraductal papillary mucinous neoplasm. DISCUSSION: We review the current literature in order to try and answer important questions regarding our ability to predict intraductal papillary mucinous neoplasm recurrence, our understanding of the potential for recurrence and what follow-up should be recommended to properly monitor recurrence after a benign, albeit borderline malignant, side-branch lesion resection. CONCLUSION: Our case report confirms that the low risk classification of an intraductal papillary mucinous neoplasm lesion even after total pancreatectomy does not always predict recurrence and that definitive prognostic factors of recurrence in the setting of non-invasive disease have yet to be identified. A vigilant long-term approach to follow-up may thus be required even in low risk cases.

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[396]

TÍTULO / TITLE: - Synergistic cytotoxicity of red beetroot (Beta vulgaris L.) extract with doxorubicin in human pancreatic, breast and prostate cancer cell lines.

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

REVISTA / JOURNAL: - J Complement Integr Med. 2013 Jun 26;10(1):1-10. doi: 10.1515/jcim-2013-0007.

●● Enlace al texto completo (gratuito o de pago) 1515/jcim-2013-0007

AUTORES / AUTHORS: - Kapadia GJ; Rao GS; Ramachandran C; Iida A; Suzuki N; Tokuda H

RESUMEN / SUMMARY: - Abstract Although a wide variety of cytotoxic plant extracts and phytochemicals are known to act synergistically with anticancer drug doxorubicin (D), their clinical application is hindered by safety concerns of such combination therapy. Our earlier studies showed that red beetroot (Beta vulgaris L.) extract (B), approved by Food and Drug Administration and European Union as red food color E162, reduced multi-organ tumor formations in various animal models when administered in drinking water. This led us to postulate that a long-term daily exposure to low doses of B through diet might be safe and sufficient to produce cancer chemopreventive effect in humans. Further, our recent comparative cytotoxic investigation with B and D in several human cancer cell lines indicated their potential for synergistic activity. Since B

is considered safe for human use with no known toxicity, we conducted the present study to evaluate its synergistic antiproliferative activity with D against pancreatic (PaCa), breast (MCF-7) and prostate (PC-3) tumor cells of human origin. Different concentrations of B and D (0.29-290 mug/ml) and in various combinations (B:D ratio = 1:0, 1:1, 5:1, 1:5 and 0:1) were tested for cytotoxic effects against the three cancer cells. The viability of cells was assessed after 72 h incubation with various combinations of B and D using the trypan-blue staining method. The cytotoxic data were analyzed by the combination index method of Chou and Talalay to establish synergy between B and D. The results indicated that an overall positive reduction in drug concentration was achieved by D when combined with B in its cytotoxicity profile in the three human cancer cells tested. The synergistic cytotoxicity was best when the B:D ratio of 1:5 was used in PaCa cells at IC50, IC75 and IC90 dose levels and in MCF-7 cells at IC90 dose level. These results warrant further studies on the potential of red beetroot extract-doxorubicin combination in treating human cancers.

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[397]

TÍTULO / TITLE: - Gemcitabine plus Nab-Paclitaxel with chemoradiation in locally advanced pancreatic cancer (LAPC).

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

REVISTA / JOURNAL: - J Gastrointest Oncol. 2013 Jun;4(2):E16-8. doi: 10.3978/j.issn.2078-6891.2013.013.

●● Enlace al texto completo (gratuito o de pago) 3978/j.issn.2078-6891.2013.013

AUTORES / AUTHORS: - Olowokure O; Torregroza-Sanchez MP; Bedoya-Apraez ID

INSTITUCIÓN / INSTITUTION: - University of Cincinnati, Department of Internal Medicine, Division of Hematology Oncology, Cincinnati OH, 45267, USA.

RESUMEN / SUMMARY: - Gemcitabine (GEM) is a cytotoxic agent that is potent against pancreatic adenocarcinoma. Nab-paclitaxel (nab-P), an albumin-bound formulation of paclitaxel, appears to decrease levels of cytidine deaminase, which is the primary gemcitabine catabolic enzyme, this likely increases sensitivity to GEM when these agents are combined. Here we present a case of a 52 year old female with locally advanced pancreatic cancer with elevated CA19-9 at diagnosis who received GEM + nab-P followed by GEM based chemoradiation who underwent surgical resection despite persistent stable disease on radiographic studies and was found to have complete pathologic response.

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[398]

TÍTULO / TITLE: - Effect of CCR7, CXCR4 and VEGF-C on the lymph node metastasis of human pancreatic ductal adenocarcinoma.

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

REVISTA / JOURNAL: - Oncol Lett. 2013 May;5(5):1572-1578. Epub 2013 Mar 15.

●● Enlace al texto completo (gratuito o de pago) 3892/ol.2013.1261

AUTORES / AUTHORS: - Guo J; Lou W; Ji Y; Zhang S

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Sixth People's Hospital Affiliated to Shanghai Jiao Tong University, Shanghai, P.R. China.

RESUMEN / SUMMARY: - The aim of the present study was to investigate the association between the expression of chemokine receptors CCR7 and CXCR4 and vascular endothelial growth factor (VEGF)-C and the lymph node metastasis of pancreatic ductal adenocarcinoma (PDAC). The mRNA transcription levels of CCR7, CXCR4 and VEGF-C were measured in 24 specimens by real-time reverse transcription (RT)-PCR, while the protein expression levels were measured in 65 specimens by immuohistochemistry. Professional software for pathological image manipulation (Image Pro Plus 6.0) was used to quantitate the results of the immunohistochemical staining. The mRNA and protein expression levels of CCR7, CXCR4 and VEGF-C were all significantly higher in the cancer samples compared with those in the adjacent normal tissue. The CCR7 and VEGF-C mRNA and protein expression levels were significantly higher in the patients with cancer types exhibiting lymph node metastasis and an advanced International Union Against Cancer (UICC) stage ($P<0.05$). The greater the number of metastatic lymph nodes, the higher the levels of CCR7 expression ($P<0.05$). There was a significant positive linear correlation between the mRNA and protein expression levels of CCR7 and VEGF-C ($P<0.05$). The mRNA and protein expression levels of CXCR4 were not correlated with the lymph node metastasis ($P>0.05$), however the strong positive expression of CCR7 and VEGF-C was significantly associated with the lymph node metastasis of PDAC.

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[399]

TÍTULO / TITLE: - A solid pancreatic mass: Tumour or inflammation?

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

REVISTA / JOURNAL: - Diagn Interv Imaging. 2013 Jul-Aug;94(7-8):741-55. doi: 10.1016/j.diii.2013.03.013. Epub 2013 Jun 7.

●● Enlace al texto completo (gratuito o de pago) 1016/j.diii.2013.03.013

AUTORES / AUTHORS: - Frampas E; Morla O; Regenet N; Eugene T; Dupas B; Meurette G

INSTITUCIÓN / INSTITUTION: - Central Radiology and Imaging Department, Hotel-Dieu, CHU de Nantes, 1, place Alexis-Ricordeau, 44093 Nantes cedex 1, France. Electronic address: eric.frampas@chu-nantes.fr.

RESUMEN / SUMMARY: - The prognosis for pancreatic cancer is poor, and early diagnosis is essential for surgical management. By comparison with its classic form, the presence of acute or chronic inflammatory signs will hinder its detection and delay its diagnosis. The atypical forms of acute pancreatitis need to be known in order to detect patients who require additional morphological

investigations to search for an underlying tumour. In contrast, pseudotumoral forms of inflammation (chronic pancreatitis, cystic dystrophy in heterotopic pancreas, autoimmune pancreatitis) may simulate a cancer, and make up 5-10% of the surgical procedures for suspected cancer. Faced with these pseudotumoral masses, interpretation relies on various differentiating signs and advances in imaging.

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[400]

TÍTULO / TITLE: - Diabetes and pancreatic cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):363-6. doi: 10.6092/1590-8577/1656.

AUTORES / AUTHORS: - El-Jurdi NH; Saif MW

INSTITUCIÓN / INSTITUTION: - Tufts University School of Medicine. Boston, MA, USA. wsaif@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - There is great emphasis on early identification of high risk patients for developing pancreatic cancer in an attempt to reduce the burden of the fourth leading cause of cancer death in the United States. Abstracts presented at the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting highlighted and supported the relationship between pancreatic cancer and diabetes mellitus and Abstract #4039 showed that hemoglobin-A1c at the time of diagnosis correlates with disease stage and predicts survival among all stages of pancreatic cancer patients. Abstracts #4044 and #e15110 also presented in 2013 ASCO Annual Meeting showed that metformin treatment serves as a positive prognosticator, especially in patients with diabetes mellitus diagnosed within 2 years of pancreatic cancer and in stage 3 pancreatic cancer patients with diabetes mellitus.

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[401]

TÍTULO / TITLE: - Hypoxia inducible factor-1 alpha plays a pivotal role in hepatic metastasis of pancreatic cancer: an immunohistochemical study.

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

REVISTA / JOURNAL: - J Hepatobiliary Pancreat Sci. 2013 Jun 20. doi: 10.1002/jhbp.6.

●● Enlace al texto completo (gratuito o de pago) 1002/jhbp.6

AUTORES / AUTHORS: - Matsuo Y; Ding Q; Desaki R; Maemura K; Mataki Y; Shinchi H; Natsugoe S; Takao S

INSTITUCIÓN / INSTITUTION: - Department of Digestive, Breast and Thyroid Surgery, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Hypoxia is an important condition to promote angiogenesis that is essential to tumor progression, including pancreatic ductal adenocarcinoma (PDAC). We evaluated whether the immunohistochemistry for hypoxia inducible factor-1alpha (HIF-1alpha) was

correlated with hepatic metastases in PDAC. METHODS: We examined the expression of HIF-1alpha, vascular endothelial growth factor-A (VEGF-A), thymidine phosphorylase (TP) and basic fibroblast growth factor (bFGF) in a total of 100 paraffin-embedded PDAC primary tumors using immunohistochemical staining, and assessed their clinicopathological correlations. We determined microvessel count (MVC) and apoptotic index (AI), and assessed their correlations with hepatic metastases. Student's t-test, the Mann-Whitney U-test, and Spearman correlation coefficients were used to validate the model, and regression analysis was used to test the model. RESULTS: Hypoxia inducible factor-1alpha expression induced the expression of multiple angiogenic factors, leading to a higher MVC and a lower AI. HIF-1alpha expression (P = 0.0087) and angiogenic factors (P = 0.0079) were significantly associated with not only the microvessel status (P = 0.022) but also the high incidence of hepatic metastasis (P = 0.02), resulting in the worse survival of PDAC patients (P < 0.05). CONCLUSIONS: Hypoxia inducible factor-1alpha plays a pivotal role in hepatic metastasis through its association with the expression of angiogenic factors in PDAC patients. These results may contribute future therapeutic strategies to prevent pancreatic cancer metastasis.

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[402]

TÍTULO / TITLE: - Collision tumors: pancreatic adenocarcinoma and mantle cell lymphoma.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):458-62. doi: 10.6092/1590-8577/1533.

AUTORES / AUTHORS: - Dasanu CA; Shimanovsky A; Rotundo EK; Posteraro AF; Cooper DL; Atienza JA

INSTITUCIÓN / INSTITUTION: - Department of Hematology-Oncology, St. Francis Hospital and Medical Center. Hartford, CT, USA. c_dasanu@yahoo.com.

RESUMEN / SUMMARY: - CONTEXT: Collision tumors are very rare entities composed of two or more distinct tumor components, each separated by normal tissue. Perhaps due to technical advances in the last decade, the incidence of collision tumors has been on the rise. To the best of our knowledge, collision tumors featuring mantle cell lymphoma and pancreatic adenocarcinoma have not been previously described in the scientific literature. CASE REPORT: For the first time, we describe herein the clinical course of a collision tumor between pancreatic adenocarcinoma and mantle cell lymphoma. DISCUSSION: We hypothesize several aspects in the pathogenesis of a such event and review the existing literature on collision tumors.

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[403]

TÍTULO / TITLE: - Duplicate pancreas meets gastric duplication cyst: A tale of two anomalies.

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

REVISTA / JOURNAL: - Int J Surg Case Rep. 2013;4(8):735-9. doi: 10.1016/j.ijscr.2013.05.005. Epub 2013 Jun 4.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ijscr.2013.05.005

AUTORES / AUTHORS: - Christians KK; Pappas S; Pilgrim C; Tsai S; Quebbeman E

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Medical College of Wisconsin, Milwaukee, WI, United States. Electronic address: kchristi@mcw.edu.

RESUMEN / SUMMARY: - INTRODUCTION: Congenital anomalies are a rare cause of pancreatitis in adults. Gastric duplications are the least common duplication of the gastrointestinal tract and are even more uncommon in the setting of a duplicate pancreas. PRESENTATION OF CASE: This manuscript contains a case report and review of the literature of an adult who presented with recurrent pancreatitis and was found to have a gastric duplication cyst that communicated with a duplicate pancreas. The study aim is to alert practitioners to the duplicate anomaly and recommend appropriate therapy. DISCUSSION: Combined gastric and pancreatic duplications usually occur in young females with nonspecific, recurrent abdominal pain. This combined duplication can result in pancreatitis when the gastric duplication is contiguous with the stomach. Heightened awareness of the condition, appropriate diagnostics with accurate interpretation and a minimalist approach to resection are warranted. CONCLUSION: Recurrent abdominal pain and pancreatitis in young adults devoid of risk factors should lead to consideration of congenital anomalies. Not all cysts near the pancreas and stomach are pseudocysts. ECRP and abdominal CT/MRI provide critical diagnostic information. This dual anomaly is best treated by simple excision of the gastric duplication and heterotopic pancreas.

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[404]

TÍTULO / TITLE: - Sarcoidosis of the pancreas mimicking adenocarcinoma.

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

REVISTA / JOURNAL: - British Medical J (BMJ). %8?(3k+]3s http://bmj.com/search.dtl ●● British Medical J. (BMJ): <> Case Rep. 2013 Jun 19;2013. pii: bcr2013009118. doi: 10.1136/bcr-2013-009118.

●● Enlace al texto completo (gratuito o de pago) 1136/bcr-2013-009118

AUTORES / AUTHORS: - Mayne AI; Ahmad J; Loughrey M; Taylor MA

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary and Pancreatic Surgery, Mater Hospital, Belfast, UK.

RESUMEN / SUMMARY: - Primary sarcoidosis of the pancreas is extremely rare. Clinical presentation is often identical to that of pancreatic adenocarcinoma. Preoperative diagnosis of primary pancreatic sarcoidosis is always challenging. We present a 52-year-old man who developed weight loss and obstructive jaundice. Abdomino-pelvic CT scan showed a mass in the pancreatic head. After hepatopancreaticobiliary MDT discussion, a Whipple's procedure was

attempted but the mass was deemed unresectable due to invasion of the superior mesenteric vein. Upon completion of palliative chemotherapy, repeat imaging showed significant mass shrinkage. A reattempt Whipple's procedure was successfully undertaken. Histology showed changes of chronic pancreatitis and peripancreatic granulomatous inflammation with no evidence of malignancy and a diagnosis of sarcoidosis was made. Owing to the devastating nature of pancreatic adenocarcinoma, any mass in the pancreas must be thoroughly investigated before a definitive diagnosis is made.

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[405]

TÍTULO / TITLE: - Pancreatic cancer: what about screening and detection?

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):312-5. doi: 10.6092/1590-8577/1645.

AUTORES / AUTHORS: - Konstantinou F; Syrigos KN; Saif MW

INSTITUCIÓN / INSTITUTION: - Oncology Unit, Third Department of Medicine, Athens School of Medicine, Sotiria General Hospital. Athens, Greece. frossokon@yahoo.gr.

RESUMEN / SUMMARY: - Pancreatic cancer is the fourth leading cause of cancer-related death in both sexes in the United States. In 2013, it is expected to account for 7% of all female cancer deaths and 6% of all male cancer deaths in the USA. Late presentation of the disease and poor prognosis even after complete operative resection, justify the necessity for early detection of pancreatic cancer as well as identifying high-risk individuals (screening). Herein, the authors summarize the data presented at the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting regarding screening and early detection of pancreatic cancer (Abstracts #4045 and #4052).

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[406]

TÍTULO / TITLE: - Biomarkers for Pancreatic Cancer: Is it Ready for Primetime?

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):309-11. doi: 10.6092/1590-8577/1676.

AUTORES / AUTHORS: - Kim R; Mahipal A; Choi M; Saif MW

INSTITUCIÓN / INSTITUTION: - H. Lee Moffitt Cancer Center. Tampa, FL, USA. richard.kim@moffitt.org.

RESUMEN / SUMMARY: - No abstract available.

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[407]

TÍTULO / TITLE: - Mucins in pancreatic cancer and its microenvironment.

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

REVISTA / JOURNAL: - Nat Rev Gastroenterol Hepatol. 2013 Jul 16. doi: 10.1038/nrgastro.2013.120.

●● Enlace al texto completo (gratuito o de pago) 1038/nrgastro.2013.120

AUTORES / AUTHORS: - Kaur S; Kumar S; Momi N; Sasson AR; Batra SK
INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, 985870 Nebraska Medical Centre, Omaha, NE 68198-5870, USA.
RESUMEN / SUMMARY: - Pancreatic cancer remains a lethal malignancy with poor prognosis owing to therapeutic resistance, frequent recurrence and the absence of treatment strategies that specifically target the tumour and its supporting stroma. Deregulated cell-surface proteins drive neoplastic transformations and are envisioned to mediate crosstalk between the tumour and its microenvironment. Emerging studies have elaborated on the role of mucins in diverse biological functions, including enhanced tumorigenicity, invasiveness, metastasis and drug resistance through their characteristic O-linked and N-linked oligosaccharides (glycans), extended structures and unique domains. Multiple mucin domains differentially interact and regulate different components of the tumour microenvironment. This Review discusses: the expression pattern of various mucins in the pancreas under healthy, inflammatory, and cancerous conditions; the context-dependent attributes of mucins that differ under healthy and pathological conditions; the contribution of the tumour microenvironment in pancreatic cancer development and/or progression; diagnostic and/or prognostic efficacy of mucins; and mucin-based therapeutic strategies. Overall, this information should help to delineate the intricacies of pancreatic cancer by exploring the family of mucins, which, through various mechanisms in both tumour cells and the microenvironment, worsen disease outcome.

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[408]
TÍTULO / TITLE: - Advances in immunotherapy for pancreatic cancer: 2013.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):347-53. doi: 10.6092/1590-8577/1646.
AUTORES / AUTHORS: - Devito NC; Saif MW
INSTITUCIÓN / INSTITUTION: - Tufts Medical Center. Boston, MA, USA. ndevito@tuftsmedicalcenter.org.
RESUMEN / SUMMARY: - Pancreatic cancer is one of the more difficult malignancies to treat, and there is a great need for less toxic, effective regimens. Immunotherapy has shown potential in the treatment of pancreatic cancer, and at ASCO 2013 there were several progressive advances in its clinical application. Abstracts #3067, #3049, #3007, #4040, #LBA4004, and #3090 will be discussed. New developments in the field of immunotherapy are promising novel treatments for pancreatic neoplasms with tolerable side effect profiles.

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[409]
TÍTULO / TITLE: - Free-breathing conformal irradiation of pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - J Appl Clin Med Phys. 2013 Jul 8;14(4):4152. doi: 10.1120/jacmp.v14i4.4152.

AUTORES / AUTHORS: - Solla I; Zucca S; Possanzini M; Piras S; Pusceddu C; Porru S; Meleddu G; Farace P

INSTITUCIÓN / INSTITUTION: - Regional Oncological Hospital. paolofarace@gmail.com.

RESUMEN / SUMMARY: - The purpose of this study was to assess treatment margins in free-breathing irradiation of pancreatic cancer after bone alignment, and evaluate their impact on conformal radiotherapy. Fifteen patients with adenocarcinoma of the head of the pancreas underwent implantation of single fiducial marker. Intrafraction uncertainties were assessed on simulation four-dimensional computed tomography (4D CT) by calculating maximal intrafraction fiducial excursion (MIFE). In the first ten patients, after bony alignment, the position of the fiducial was identified on weekly acquired megavolt cone-beam CT (MV-CBCT). The interfraction residual uncertainties were estimated by measuring the fiducial displacements with respect to the position in the first session. Patient mean (pM) and patient standard deviation (pSD) of fiducial displacement, mean (muM) and standard deviation (muSD) of pM, and root-mean-square of pSD (sigmares) were calculated. In the other five patients, MIFE was added to the residual component to obtain personalized margin. In these patients, conformal kidney sparing (CONKISS) irradiation was planned prescribing 54/45 Gy to PTV1/PTV2. The organ-at-risk limits were set according to current NCCN recommendation. No morbidity related to the fiducial marker implantation was recorded. In the first ten patients, along right-left, anterior-posterior, and inferior-superior directions, MIFE was variable (mean +/- std = 0.24 +/- 0.13cm, 0.31 +/- 0.14 cm, 0.83 +/- 0.35 cm, respectively) and was at most 0.51, 0.53, and 1.56 cm, respectively. Along the same directions, muM were 0.09, -0.05, -0.05 cm, muSD were 0.30, 0.17, 0.33 cm, and sigmares were 0.35, 0.26, and 0.30 cm, respectively. MIFE was not correlated with pM and pSD. In the five additional patients, it was possible to satisfy recommended dose limits, with the exception of slightly higher doses to small bowel. After bony alignment, the margins for target expansion can be obtained by adding personalized MIFE to the residual interfraction term. Using these margins, conformal free-breathing irradiation is a reliable option for the treatment of pancreatic cancer.

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[410]

TÍTULO / TITLE: - Solid pseudopapillary neoplasm of the pancreas.

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

REVISTA / JOURNAL: - Diagn Interv Imaging. 2013 May 29. pii: S2211-5684(13)00138-1. doi: 10.1016/j.diii.2013.04.005.

●● Enlace al texto completo (gratuito o de pago) 1016/j.diii.2013.04.005

AUTORES / AUTHORS: - Klotz T; Da Ines D; Petitcolin V; Lannareix V; Essamet W; Garcier JM

INSTITUCIÓN / INSTITUTION: - Department of Radiology and Medical Imaging, CHU Clermont-Ferrand, CHU Estaing, 1, place Lucie-Aubrac, 63003 Clermont-Ferrand cedex 1, France.

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[411]

TÍTULO / TITLE: - Pancreatic pseudocyst with fistula to the common bile duct and the duodenum.

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

REVISTA / JOURNAL: - Nihon Shokakibyo Gakkai Zasshi. 2013 Jul;110(7):1288-95.

AUTORES / AUTHORS: - Doi T; Wakabayashi N; Iwai N; Morita Y; Ogiso K; Fujii K; Takada R; Takaya H; Masuzawa A; Matsumoto N; Takami S; Kataoka K

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology and Hepatology, Otsu Municipal Hospital.

RESUMEN / SUMMARY: - A 35-year-old man was hospitalized for severe acute pancreatitis. On the 24th hospital day, CT scan showed a pancreatic pseudocyst in the head of the pancreas. Conservative medical treatment for 1 month was not effective, and CT scan revealed a fistulous communication of the pseudocyst to the common bile duct and duodenum. After the formation of a fistulous communication, we detected common bile duct stones composed of fatty acid calcium and we removed them endoscopically. The pseudocyst gradually decreased in size and disappeared 4 months later. Follow-up CT scan showed no sign of recurrence.

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[412]

TÍTULO / TITLE: - Huge mucinous cystadenoma of the pancreas mistaken for a pseudocyst.

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

REVISTA / JOURNAL: - Pan Afr Med J. 2013 May 3;15:6. doi: 10.11604/pamj.2013.15.6.2494. Print 2013.

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

11604/pamj.2013.15.6.2494

AUTORES / AUTHORS: - Olaoye IO; Adesina MD

INSTITUCIÓN / INSTITUTION: - University Of Ilorin Teaching Hospital, Nigeria.

RESUMEN / SUMMARY: - Cystic tumors of the pancreas are rare and can be confused with pseudocysts.We present a 50 year old woman with a huge mucinous cystadenoma of the pancreas initially diagnosed and managed with a cystojejunostomy and cyst wall biopsy. She required another laparotomy and tumor excision after histological diagnosis. Sensitivity of radiological imaging in differentiating between cystic pancreatic tumors and pseudocysts is limited. Cyst wall histology is diagnostic and biopsy of cyst wall should be done in cases with inconclusive preoperative diagnosis or questionable operative findings.

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[413]

TÍTULO / TITLE: - Pancreatic serous cystadenoma with signs of compression.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Diagn Interv Imaging. 2013 Jun 18. pii: S2211-5684(13)00158-7. doi: 10.1016/j.diii.2013.04.017.

●● Enlace al texto completo (gratuito o de pago) 1016/j.diii.2013.04.017

AUTORES / AUTHORS: - Feldis M; Marty M; Dilly M; Laurent F; Chiche L; Cassinotto C

INSTITUCIÓN / INSTITUTION: - Abdominal, gastro-intestinal and endocrine radiology unit, Haut-Leveque Hospital, Sud Hospital Group, Bordeaux University Hospital, 1, avenue de Magellan, 33604 Pessac cedex, France. Electronic address: matthieu.feldis@gmail.com.

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[414]

TÍTULO / TITLE: - Comparison of capecitabine and 5-fluorouracil in chemoradiotherapy for locally advanced pancreatic cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Radiat Oncol. 2013 Jul 3;8(1):160.

●● Enlace al texto completo (gratuito o de pago) 1186/1748-717X-8-160

AUTORES / AUTHORS: - Kim YJ; Lee WJ; Woo SM; Kim TH; Han SS; Kim BH; Moon SH; Kim SS; Koh YH; Park SJ; Kim JY; Kim DY; Park JW

RESUMEN / SUMMARY: - BACKGROUND: Although capecitabine has theoretical advantages in the pharmacokinetics, such as higher intratumoral and lower systemic concentration, relative to bolus 5-fluorouracil (5-FU), outcomes of chemoradiotherapy (CRT) with capecitabine or bolus 5-FU have not been directly compared in patients with locally advanced pancreatic cancer. Therefore, we retrospectively compared the outcomes, including toxicity, tumor response, and overall survival, of oral capecitabine plus radiotherapy (RT) with bolus 5-FU plus RT, in patients with locally advanced pancreatic cancer. METHODS: Between August 2006 and January 2012, 98 patients with locally advanced pancreatic cancer received CRT, with 52 receiving concurrent oral capecitabine and 46 receiving bolus injection of 5-FU. Primary tumor and overall response after CRT were evaluated radiologically, and toxicity, tumor response, and overall survival (OS) were compared in the two groups. RESULTS: Baseline clinical parameters of the two groups were similar. The rates of >= Grade 3 hematologic (0% vs. 8.7%, p = 0.045) and non-hematologic (0% vs. 8.7%, p = 0.045) toxicities were significantly lower in the capecitabine group than in the 5-FU group. Primary tumor (30.7% vs. 28.2%, p = 0.658) and overall (13.7% vs. 15.2%, p = 0.273) response rates and median OS time (12.5 months vs. 11.6 months, p = 0.655) were similar in the two groups. CONCLUSIONS: Capecitabine plus RT maybe a safe and feasible regimen for patients with locally advanced pancreatic cancer, with similar efficacy and low rates of toxicities compared with bolus 5-FU plus RT.

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[415]

TÍTULO / TITLE: - Squamous cell carcinoma of the pancreas.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Arch Iran Med. 2013 Jun;16(6):369-70. doi: 013166/AIM.0012.
AUTORES / AUTHORS: - Nikfam S; Sotoudehmanesh R; Pourshams A; Sadeghipour A; Sotoudeh M; Mohamadnejad M
INSTITUCIÓN / INSTITUTION: - Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, Iran.
RESUMEN / SUMMARY: - Squamous cell carcinoma (SCC) of the pancreas is a controversial entity of uncertain origin, as the pancreas is entirely devoid of squamous cells. Cases of pancreatic carcinomas that exhibit primary squamous morphology are rarely described in the literature. We report a case of primary SCC of the pancreas in a 66-year-old woman with complaints of epigastric pain of five months duration. Imaging studies demonstrated a solid tumor in the body of the pancreas that invaded the superior mesenteric (SMA) and celiac arteries, as well as regional lymph nodes. Cytological examination of an endosonography-guided fine needle aspiration (EUS-FNA) specimen confirmed the diagnosis of well-differentiated SCC of the pancreas. On the basis of diagnosis and examinations prior to chemotherapy, we did not detect any SCC lesions that might have metastasized to the pancreas. Primary SCC of the pancreas is a rare entity that comprises 0.05% of all exocrine pancreatic carcinomas. The clinical profile and biological behavior of pancreas SCC are similar to typical pancreatic ductal adenocarcinomas.

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[416]
TÍTULO / TITLE: - Metastatic Pancreatic Cancer: The Dilemma of Quality vs. Quantity of Life.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):391-4. doi: 10.6092/1590-8577/1663.
AUTORES / AUTHORS: - Shahrokni A; Saif MW
INSTITUCIÓN / INSTITUTION: - University of California. Los Angeles, CA, USA. ashahrokni@mednet.ucla.edu.
RESUMEN / SUMMARY: - Due to pancreatic cancer's dismal prognosis, much of management is focused upon palliation and symptom management, and the decision to treat a patient with more aggressive maneuvers must always take into account the impact upon a patient's quality of life. In addition, majority of the patients with advanced pancreatic cancer are elderly. Oncologists are challenged to make tough treatment decisions. Many elderly patients cannot tolerate side effects of chemotherapy, especially the combination regimens. Despite that many patients continue to receive chemotherapy even in the last month of their lives. The effect of referral to palliative care on health-related outcome especially for patients with poor quality of life is still not very clear. The authors will review abstracts that have focused on these fields that were

presented at the Annual Meeting of ASCO 2013 (Abstracts #4009, #4053, #6607, #9518, #9538, #9539, #9546, and #9638).

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[417]

TÍTULO / TITLE: - Bioluminescent orthotopic model of pancreatic cancer progression.

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

REVISTA / JOURNAL: - J Vis Exp. 2013 Jun 28;(76). doi: 10.3791/50395.

●● Enlace al texto completo (gratuito o de pago) 3791/50395

AUTORES / AUTHORS: - Chai MG; Kim-Fuchs C; Angst E; Sloan EK

INSTITUCIÓN / INSTITUTION: - Monash Institute of Pharmaceutical Sciences, Monash University.

RESUMEN / SUMMARY: - Pancreatic cancer has an extremely poor five-year survival rate of 4-6%. New therapeutic options are critically needed and depend on improved understanding of pancreatic cancer biology. To better understand the interaction of cancer cells with the pancreatic microenvironment, we demonstrate an orthotopic model of pancreatic cancer that permits non-invasive monitoring of cancer progression. Luciferase-tagged pancreatic cancer cells are resuspended in Matrigel and delivered into the pancreatic tail during laparotomy. Matrigel solidifies at body temperature to prevent leakage of cancer cells during injection. Primary tumor growth and metastasis to distant organs are monitored following injection of the luciferase substrate luciferin, using in vivo imaging of bioluminescence emission from the cancer cells. In vivo imaging also may be used to track primary tumor recurrence after resection. This orthotopic model is suited to both syngeneic and xenograft models and may be used in pre-clinical trials to investigate the impact of novel anti-cancer therapeutics on the growth of the primary pancreatic tumor and metastasis.

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[418]

TÍTULO / TITLE: - Multiple cardiac metastases from a nonfunctioning pancreatic neuroendocrine tumor.

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

REVISTA / JOURNAL: - Cancer Res. %2!?[y+9?%ak http://cancerres.aacrjournals.org/ ●● Cancer Research: <> Treat. 2013 Jun;45(2):150-4. doi: 10.4143/crt.2013.45.2.150. Epub 2013 Jun 30.

●● Enlace al texto completo (gratuito o de pago) 4143/crt.2013.45.2.150

AUTORES / AUTHORS: - Choi YH; Han HS; Lim SN; Lee SY; Koo JH; Lee OJ; Lee KH; Kim ST

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Chungbuk National University College of Medicine, Cheongju, Korea.

RESUMEN / SUMMARY: - Pancreatic neuroendocrine tumors (pNETs) are rare neoplasms, which most commonly metastasize to the liver. However, intrathoracic metastases from pNETs are encountered infrequently. This report describes a case of nonfunctioning pNET with multiple cardiac metastases. A

56-year-old male presented with a palpable abdominal mass that showed progressive enlargement. Findings on computed tomography (CT) of the abdomen revealed two relatively well-marginated inhomogeneous low-attenuation masses, one in the head of the pancreas and the other in the tail. Multiple enhancing masses in the left pericardium with myocardial involvement were observed on chest CT and transthoracic echocardiography. Needle biopsies were performed on the mass in the tail of the pancreas and the left ventricular apical pericardium; histologic examination by hematoxylin and eosin morphology and immunohistochemical staining showed pNET in both. This is the first report of pNET with multiple cardiac metastases to previously undescribed metastatic sites.

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[419]

TÍTULO / TITLE: - A novel epigenetic CREB-miR-373 axis mediates ZIP4-induced pancreatic cancer growth.

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

REVISTA / JOURNAL: - EMBO Mol Med. 2013 Jul 16. doi: 10.1002/emmm.201302507.

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

1002/emmm.201302507

AUTORES / AUTHORS: - Zhang Y; Yang J; Cui X; Chen Y; Zhu VF; Hagan JP; Wang H; Yu X; Hodges SE; Fang J; Chiao PJ; Logsdon CD; Fisher WE; Brunicardi FC; Chen C; Yao Q; Fernandez-Zapico ME; Li M

INSTITUCIÓN / INSTITUTION: - Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX, USA.

RESUMEN / SUMMARY: - Changes in the intracellular levels of the essential micronutrient zinc have been implicated in multiple diseases including pancreatic cancer; however, the molecular mechanism is poorly understood. Here, we report a novel mechanism where increased zinc mediated by the zinc importer ZIP4 transcriptionally induces miR-373 in pancreatic cancer to promote tumour growth. Reporter, expression and chromatin immunoprecipitation assays demonstrate that ZIP4 activates the zinc-dependent transcription factor CREB and requires this transcription factor to increase miR-373 expression through the regulation of its promoter. miR-373 induction is necessary for efficient ZIP4-dependent enhancement of cell proliferation, invasion, and tumour growth. Further analysis of miR-373 in vivo oncogenic function reveals that it is mediated through its negative regulation of TP53INP1, LATS2 and CD44. These results define a novel ZIP4-CREB-miR-373 signalling axis promoting pancreatic cancer growth, providing mechanistic insights explaining in part how a zinc transporter functions in cancer cells and may have broader implications as inappropriate regulation of intracellular zinc levels plays an important role in many other diseases.

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[420]

TÍTULO / TITLE: - BRCA and Pancreatic Cancer.

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

REVISTA / JOURNAL: - JOP. 2013 Jul 10;14(4):325-8. doi: 10.6092/1590-8577/1652.

AUTORES / AUTHORS: - Brennan GT; Relias V; Saif MW

INSTITUCIÓN / INSTITUTION: - Division of GI Oncology and Experimental Therapeutics, Tufts Medical Center. Boston, MA, USA. vrelias1@tuftsmedicalcenter.org.

RESUMEN / SUMMARY: - Germline mutations in BRCA genes have been associated with pancreatic cancer. Laboratory and clinical data suggest that patients with BRCA mutations may be more responsive to therapy consisting of conventional chemotherapy with a poly(ADP-ribose) polymerase inhibitor (PARPi). The most recent data from the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting will be reviewed (Abstracts #11024 and #TPS4144).
